Docket No. ST98007 US

8-23-00

PATENT A

PATENT APPLICATION TRANSMITTAL

Commissioner for Patents
Washington, D.C. 20231

Transmitted herewith for filing is the patent application under 37 CFR 1.53(b) of:

INVENTORS: DESMAZEAU ET AL

FOR: STREPTOGRAMIN DERIVATIVES, PREPARATION METHOD AND COMPOSITIONS CONTAINING SAME

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EL620187425US
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☒ If a CONTINUING Application, check appropriate box and supply the requisite information:
☒ Continuation ☐ Divisional ☐ Continuation-in-part
of prior application no: PCT/FR99/00409, filed 24 February 1999.
(The cross reference has been/will be inserted on page one of the specification).

☒ This application claims priority from French Patent Application No. FR98-02316 dated 26 February 1998). (The cross reference has been/will be inserted on page one of the specification).

Enclosed are:

☒ Specification [Total Pages 285]

☐ Sheets/Pages of Drawing.

☐ Nucleotide and/or Amino Acid Sequence Submission:
☐ Computer Readable Copy ☐ Paper Copy ☐ Statement verifying identity of said copies.

☒ A Declaration ☒ Unexecuted
☐ Copy from a prior application (37 CFR 1.63(d))

☐ ***Incorporation By Reference*** (useable if filing a continuation/divisional and a copy of the declaration from the prior application is enclosed.)
The entire disclosure of the prior application, from which a copy of the oath or declaration is supplied, is considered as being part of the disclosure of the accompanying application and is hereby incorporated by reference therein.

☒ Also enclosed:
Postcard
Print EFS
Preliminary Amendment

☐ This application is filed by fewer than all the inventors named in the prior application.

☐ DELETE the following inventor(s) named in the prior nonprovisional application:

_____

_____

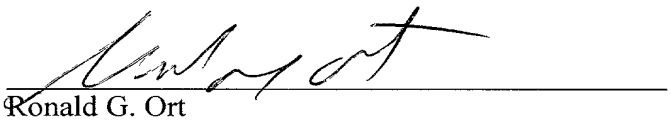
_____

CLAIMS AS FILED				
(1) FOR	(2) NUMBER FILED	(3) NUMBER EXTRA	(4) RATE	(5) BASIC FEE ($690.00)
TOTAL CLAIMS	17	0	x $ 18.00	0.00
INDEPENDENT CLAIMS	1	0	x $ 78.00	0.00
MULTI-DEPENDENT CLAIMS(S), Per Application ($260.00)				
			TOTAL FILING FEE	$690.00

☐ Cancel in this application original claims _____ of the prior application before calculating the filing fee. (At least one original independent claim has been retained for filing purposes)

☒ Please charge my Deposit Account No. **18-1982** in the amount of $690.00. A duplicate copy of this sheet is enclosed.

☒ The Commissioner is hereby authorized to charge any fees under 37 C.F.R. 1.16 and 1.17 which may be required by this paper, or credit any overpayment to Account No. **18-1982**. A duplicate copy of this sheet is enclosed.



Ronald G. Ort
Attorney/Agent for Applicant
Registration No. 26,969

Customer No.005487
Aventis Pharmaceuticals Inc.
Patent Department; Mail Stop: EMC-G1
Route #202-206 / P.O. Box 6800
Bridgewater, NJ 08807-0800
Telephone (908) 231-**4656**
Telefax (908) 231-2626

Docket No. ST98007 US

INVENTOR INFORMATION

Inventor One Given Name:: Pascal
Family Name:: Desmazeau
Postal Address Line One:: 45 rue des Marronniers
City:: 91250 Tigery
Country:: France
Postal or Zip Code:: 91250
City of Residence:: 91250 Tigery
Country of Residence:: France
Citizenship Country:: France
Inventor Two Given Name:: Gilles
Family Name:: Doerflinger
Postal Address Line One:: Residence Les Millepertuis, Bat. B3
City:: Les Ulis
Country:: France
Postal or Zip Code:: 91940
City of Residence:: Les Ulis
Country of Residence:: France
Citizenship Country:: France
Inventor Three Given Name:: Yves
Family Name:: Ribeill
Postal Address Line One:: 313 Meeting House Circle
City:: Raleigh
State or Province:: North Carolina
Country:: US
Postal or Zip Code:: 27615
City of Residence:: Raleigh
State or Province of Residence:: North Carolina
Country of Residence:: US
Citizenship Country:: France
Inventor Four Given Name:: Eric
Family Name:: Bacque
Postal Address Line One:: 19 rue Colas
City:: Morsang Sur Orge
Country:: France
Postal or Zip Code:: 91390
City of Residence:: Morsang Sur Orge
Country of Residence:: France
Citizenship Country:: France
Inventor Five Given Name:: Jean-Claude
Family Name:: Barriere
Postal Address Line One:: 24 rue Max Ernst
City:: Bures Sur Yvette
Country:: France
Postal or Zip Code:: 91400
City of Residence:: Bures Sur Yvette
Country of Residence:: France
Citizenship Country:: France
Inventor Six Given Name:: Gilles

Family Name:: Dutruc-Rosset
Postal Address Line One:: 21 avenue du docteur Arnold Netter
City:: Paris
Country:: France
Postal or Zip Code:: 75012
City of Residence:: Paris
Country of Residence:: France
Citizenship Country:: France
Inventor Seven Given Name:: Gerard
Family Name:: Puchault
Postal Address Line One:: 7 rue des Marguilliers
City:: Marcilly
Country:: France
Postal or Zip Code:: 77139
City of Residence:: Marcilly
Country of Residence:: France
Citizenship Country:: France

CORRESPONDENCE INFORMATION

Correspondence Customer Number:: 005487
Fax One:: 908-231-2626
Electronic Mail One:: ronald.ort@aventis.com

APPLICATION INFORMATION

Title Line One:: STREPTOGRAMIN DERIVATIVES, PREPARATION M
Title Line Two:: ETHOD AND COMPOSITIONS CONTAINING SAME
Total Drawing Sheets:: 0
Formal Drawings?:: No
Application Type:: Utility
Docket Number:: ST98007-US
Secrecy Order in Parent Appl.?:: No

REPRESENTATIVE INFORMATION

Representative Customer Number:: 5487

CONTINUITY INFORMATION

This application is a:: CONTINUATION OF
> Application One:: PCT/FR99/00409
Filing Date:: 02-24-1999

PRIOR FOREIGN APPLICATIONS

Foreign Application One:: FR98/02316
Filing Date:: 02-26-1998

Country:: France
Priority Claimed:: Yes

Source:: PrintEFS Version 1.0.1

Aventis File No.: ST98007 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:	**DESMAZEAU et al;.**	Group Art Unit:	**Unknown**
Serial No.:	**TBA**	Examiner:	**Unknown**
Filed:	**Concurrently**		
For:	**STREPTOGRAMIN DERIVATIVES, PREPARATION METHOD AND COMPOSITIONS CONTAINING SAME**		

CERTIFICATE OF MAILING (37 CFR 1.8a)

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Ronald G. Ort

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Box: Application
Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Please amend the application as follows:

Page 1, after Title, insert:

This application is a continuation of PCT/FR99/00409, filed February 24, 1999, which claims priority from French Application No. FR98/02316, filed February 26, 1998.

Respectfully submitted,

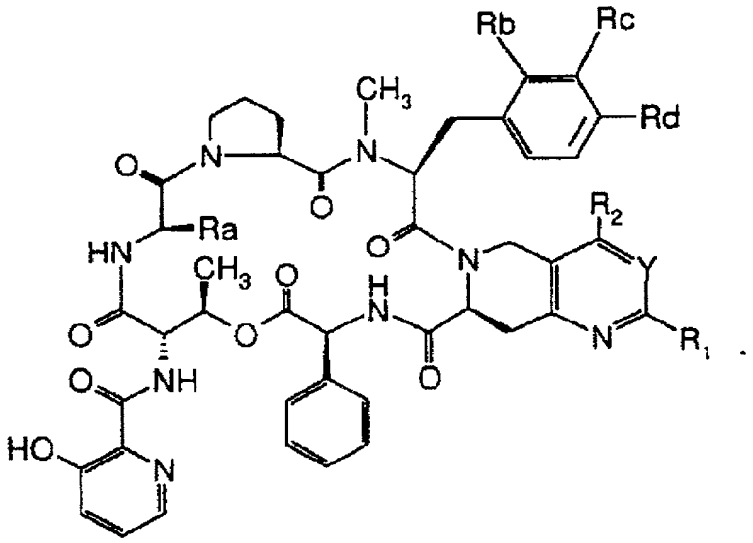
Dated:

Ronald G. Ort
Attorney for Applicant
Registration No. 26,969

Customer No. 005487
Aventis Pharmaceuticals Inc.
Patent Department; Mail Stop: EMC-G1
Route #202-206 / P.O. Box 6800
Bridgewater, NJ 08807-0800
Telephone (908) 231-**4656**
Telefax (908) 231-2626

STREPTOGRAMIN DERIVATIVES, PREPARATION METHOD AND COMPOSITIONS CONTAINING SAME

The present invention relates to group B streptogramin derivatives of general formula:



in which

Y is a nitrogen atom or a radical $=CR_3-$,

R_1 is a hydrogen atom, a radical alkyl (1 to 8 carbons), alkenyl (2 to 8 carbons), cycloalkyl (3 to 8 carbons), heterocyclyl which is saturated or unsaturated (3 to 8 members), phenyl, phenyl which is substituted [with one or more halogen atoms or hydroxyl, alkyl, alkyloxy, alkylthio, alkylsulphinyl, alkylsulphonyl, amino, alkylamino or dialkylamino radicals] or a radical NR'R", R' and R", which are identical or different, being capable of being hydrogen atoms or alkyl radicals (1 to 3 carbons), or being capable of forming together

with the nitrogen atom to which they are attached a 3- to 8-membered heterocycle optionally containing another heteroatom chosen from oxygen, sulphur or nitrogen which is optionally substituted [with a radical alkyl, alkenyl (2 to 8 carbons), cycloalkyl (3 to 6 carbons), heterocyclyl which is saturated or unsaturated (4 to 6 members), benzyl, phenyl or phenyl which is substituted as defined above for the definition of R_1] or alternatively when Y is a radical $=CR_3-$, R_1 may also be halomethyl, hydroxymethyl, alkyloxymethyl, alkylthiomethyl in which the alkyl portion is optionally substituted with NR'R", alkylsulphinylmethyl, alkylsulphonylmethyl, acyloxymethyl, benzoyloxymethyl, cyclopropylaminomethyl or $-(CH_2)_nNR'R"$ (n being an integer from 1 to 4 and R' and R" being defined as above), or alternatively if R_3 is a hydrogen atom, R_1 may also be formyl, carboxyl, alkyloxycarbonyl, or -CONR'R" for which R' and R" are defined as above,

or alternatively when Y is a nitrogen atom, R_1 may also be a radical $-XR^\circ$ for which X is an oxygen or sulphur atom, a sulphinyl or sulphonyl radical, or an NH radical and R° is a radical alkyl (1 to 8 carbons), cycloalkyl (3 to 6 carbons), heterocyclyl which is saturated or unsaturated (3 to 8 members), heterocyclylmethyl (3 to 8 members) in which the heterocyclyl portion is attached to the methyl radical by a carbon atom, phenyl, phenyl which is substituted

[with one or more halogen atoms or hydroxyl, alkyl, alkyloxy, alkylthio, alkylsulphinyl, alkylsulphonyl, amino, alkylamino or dialkylamino radicals] or a radical $-(CH_2)_nNR'R"$ for which R' and R" are defined as above and n is an integer from 2 to 4, or alternatively if X represents NH, R° may also represent the hydrogen atom,

R_2 is a hydrogen atom or an alkyl radical (1 to 3 carbons),

R_3 is a hydrogen atom or an alkyl, carboxyl, alkyloxycarbonyl or carbamoyl radical having the structure -CO-NR'R" in which R' and R" are defined as above,

Ra is a methyl or ethyl radical, and

Rb, Rc and Rd have the definitions below:

1) Rb and Rc are hydrogen atoms and Rd is a hydrogen atom or a methylamino or dimethylamino radical,

2) Rb is a hydrogen atom, Rc is a hydrogen, chlorine or bromine atom, or represents an alkenyl radical (3 to 5C), and Rd is a radical -NMe-R"' for which R"' represents a radical alkyl, hydroxyalkyl (2 to 4C), or alkenyl (2 to 8C) which is optionally substituted with phenyl, cycloalkyl(3 to 6C)methyl, benzyl, benzyl which is substituted [with one or more halogen atoms or hydroxyl, alkyl, alkyloxy, alkylthio, alkylsulphinyl, alkylsulphonyl, amino, alkylamino or dialkylamino radicals], heterocyclylmethyl or heterocyclylethyl

in which the heterocyclyl portion is saturated or unsaturated and contains 5 to 6 members and 1 or 2 heteroatoms chosen from sulphur, oxygen or nitrogen which is optionally substituted [with a radical alkyl, alkenyl (2 to 8 carbons), cycloalkyl (3 to 6 carbons), heterocyclyl which is saturated or unsaturated (4 to 6 members), phenyl, phenyl which is substituted as defined above for the definition of R_1 or benzyl], or alternatively R"' represents a radical cyanomethyl, or $-CH_2CORe$ for which either Re is -OR'e, R'e being hydrogen, alkyl (1 to 6 carbons), alkenyl (2 to 6 carbons), benzyl or heterocyclylmethyl in which the heterocyclyl portion contains 5 to 6 members and 1 or 2 heteroatoms chosen from sulphur, oxygen or nitrogen, or Re is an alkylamino, alkylmethylamino, heterocyclylamino or heterocyclylmethylamino radical in which the heterocyclyl portion is saturated and contains 5 to 6 members and 1 or 2 heteroatoms chosen from sulphur, oxygen or nitrogen which is optionally substituted with an alkyl, benzyl or alkyloxycarbonyl radical,

3) Rb is a hydrogen atom, Rd is a radical $-NHCH_3$ or $-N(CH_3)_2$ and Rc is a chlorine or bromine atom, or represents an alkenyl radical (3 to 5C), [if Rd is $-N(CH_3)_2$],

4) Rb and Rd are hydrogen atoms and Rc is a halogen

atom, or an alkylamino or dialkylamino, alkyloxy, trifluoromethoxy, thioalkyl, alkyl (1 to 6C) or trihalomethyl radical,

5) Rb and Rc are hydrogen atoms and Rd is a halogen atom, or an ethylamino, diethylamino or methylethylamino, alkyloxy or trifluoromethoxy, alkylthio, alkylsulphinyl, alkylsulphonyl, alkyl (1 to 6C), phenyl or trihalomethyl radical,

6) Rb is a hydrogen atom and Rc is a halogen atom or an alkylamino or dialkylamino, alkyloxy or trifluoromethoxy, thioalkyl or alkyl (1 to 3C) radical, and Rd is a halogen atom or an amino, alkylamino or dialkylamino, alkyloxy or trifluoromethoxy, thioalkyl, alkyl (1 to 6C) or trihalomethyl radical,

7) Rc is a hydrogen atom and Rb and Rd represent a methyl radical,

as well as their salts, which exhibit a particularly advantageous antibacterial activity, alone or combined with a group A streptogramin derivative.

In the general formula (I) above, the halogen atoms may be chosen from fluorine, chlorine, bromine or iodine; the alkyl or acyl radicals are straight or branched and, unless otherwise stated, contain 1 to 4 carbon atoms. The same is true for the alkyl radicals which will be mentioned below. The alkenyl radicals may also be in the form of a straight or branched chain.

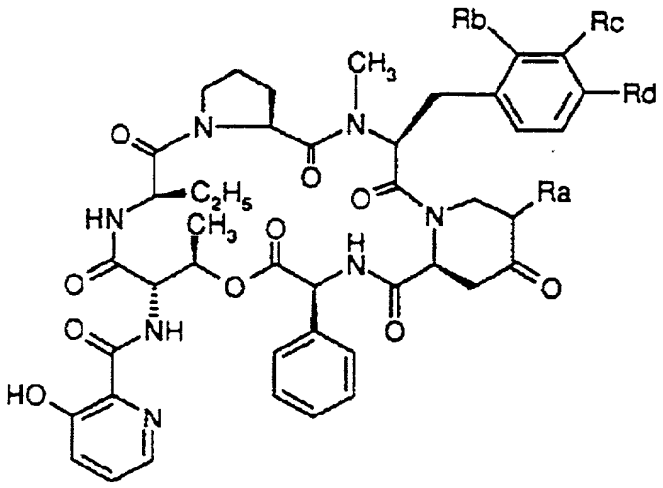
Moreover, by way of example, when R' and R"

together form a heterocycle with the nitrogen atom to which they are attached, the latter contains 1 or 2 heteroatoms and may for example be chosen from pyrrolidinyl, piperidino, morpholino, thiomorpholino, piperazinyl, methyl piperazinyl, imidazolidinyl, methylimidazolidinyl. By way of example, when R_1 or R^o represents heterocyclyl, when -NR'R" and/or R"' are substituted with heterocyclyl or when R"' represents heterocyclylmethyl, the heterocyclyl radical contains 1 or 2 heteroatoms and may for example be chosen from pyridyl, pyrazinyl, pyrimidinyl, thienyl, furyl, imidazolyl, which are optionally substituted, or from the heterocycles mentioned above at a preference for -NR'R".

Among the known streptogramins, pristinamycin (RP 7293), an antibacterial of natural origin produced by *Streptomyces pristinaespiralis* was first isolated in 1955. The pristinamycin marketed under the name Pyostacine® consists mainly of pristinamycin I_A combined with pristinamycin II_A.

Another antibacterial of the class of streptogramins: virginiamycin, has been prepared from *Streptomyces virginiae*, ATCC 13161 [Antibiotics and Chemotherapy, 5, 632 (1955)]. Virginiamycin (Staphylomycin®) consists mainly of the factor S combined with factor M_1.

Semisynthetic derivatives of streptogramins represented by the structure:



(A)

in which,

Ra is a radical having the structure $-CH_2R'a$ for which R'a is a radical of the heterocyclylthio type which may be substituted or alternatively represents a radical having the structure =CHR'a for which R'a is an alkylamino, alkyloxy or alkylthio radical which are substituted, or a radical of the heterocyclylamino, heterocyclyloxy or heterocyclylthio type which may be substituted, Rb and Rc are hydrogen atoms and Rd is a hydrogen atom or a dimethylamino radical, or alternatively

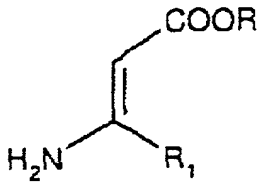
Ra is a hydrogen atom and Rb is hydrogen or methyl, Rc and Rd are hydrogen or various substituents

have been described in patents or patent applications EP 133097, EP 248703, EP 770132 and EP 772630. Combined with a semisynthetic component of the group A streptogramins, they manifest a synergistic action and can be used as antibacterial agents either by the injection route alone, or solely by the oral route.

The streptogramin derivatives of general

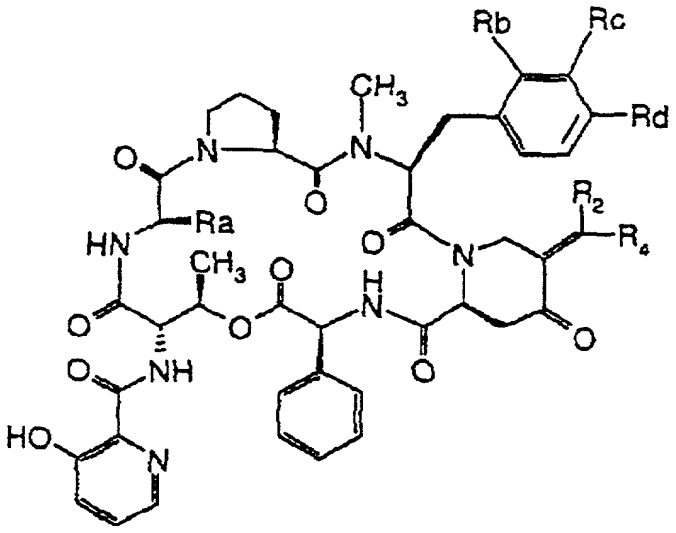
formula (I) are particularly advantageous because of their potent activity both by the oral and parenteral routes, which offers them an undeniable advantage in the case especially of treatments of serious infections, in a hospital setting by the injection route, followed by an ambulatory treatment by the oral route which is easier to administer to patients. Thus, the practitioner is no longer obliged to change the patient's medicament between the end of the hospital treatment and the overall end of the treatment.

According to the invention, the streptogramin derivatives for which Y is a radical $=CR_3-$ and R_3 is other than an alkyl radical may be prepared by the action of an enamino ester of general formula:



(II)

in which R_1 is defined as above and R represents the residue of an easily hydrolysable ester or an alkyl radical, on the corresponding 5δ-methylenepristinamycin derivative of general formula:



(III)

in which Ra, Rb, Rc and Rd are defined as above, R_2 is defined as above and R_4 is a hydrogen atom, or R_2 represents a hydrogen atom and R_4 is a hydrogen atom or a dialkylamino radical, followed where appropriate by the conversion of the ester obtained to an acid, and then optionally by its decarboxylation, or by the conversion of the acid to a carbamoyl radical according to the derivative of general formula (I) desired, and/or followed where appropriate by the conversion of the derivative of general formula (I) for which R_1 is hydroxymethyl to a derivative for which R_1 is a radical formyl, and then where appropriate carboxyl, and then where appropriate alkyloxycarbonyl or -CONR'R" and/or optionally followed by the mono- N-demethylation of the derivative of general formula (I) for which Rd is a dimethylamino radical to a derivative for which Rd is methylamino, and then optionally followed by the conversion to a salt when they exist.

Residue of an easily hydrolysable ester is

understood to mean, for example and with no limitation being implied, the residue of the benzyl, methyl, trimethylsilylethyl, ethyl, allyl or t-butyl ester.

The reaction is generally carried out in an organic solvent such as an alcohol for example (methanol, ethanol in particular), at a temperature of between 40°C and the reflux temperature of the reaction mixture.

The conversion to an acid, an amide, or the decarboxylation in order to obtain a derivative in which R_3 is carboxyl, carbamoyl having the structure -CO-NR'R" or a hydrogen atom, is carried out according to known methods which do not adversely affect the rest of the molecule and more particularly according to the methods mentioned below in the examples.

In particular, when it is desired to obtain a pristinamycin derivative of general formula (I) for which R_3 is a carboxyl radical, the benzyl ester is advantageously prepared. The hydrolysis of the esters is carried out according to known methods which do not adversely affect the rest of the molecule, for example the methods mentioned by T.W. Greene Protective Groups in Organic Synthesis, A. Wiley - Interscience Publication (1981), or by Mc Omie, Protective Groups in Organic Chemistry, Plenum Press (1973). By way of example, the residue of the benzyl ester may be hydrolysed by treatment with 1,4-cyclohexadiene in the presence of palladium hydroxide on carbon, in an

alcoholic medium (methanol, ethanol for example), at a temperature of between 0 and 60°C.

When it is desired to prepare a derivative of general formula (I) for which R_3 is -CO-NR'R", the product of general formula (I) obtained for which R_3 is carboxyl is treated according to the usual methods for converting acids to amides, which do not adversely affect the rest of the molecule. In particular, the corresponding amine is reacted with the acid in the presence of a condensing agent (carbodiimide for example) at a temperature of between 0 and 60°C, in an organic solvent such as a chlorinated solvent (chloroform, dichloromethane for example), an amide (dimethylformamide, N-methylpyrrolidone for example).

When it is desired to obtain a streptogramin derivative of general formula (I) for which R_3 is a hydrogen atom, the product for which R_3 is carboxyl is decarboxylated according to the customary methods which do not adversely affect the rest of the molecule. In particular, the procedure may be carried out according to the method described by Barton, Tetrahedron, 44(17), 5479-86 (1988), by formation of the N-hydroxypyridine-2-thione ester, and then photolysis in the presence of tert-butylthiol for example.

The mono-N-demethylation of the streptogramin derivative of general formula (I) for which Rd is dimethylamino may be carried out according to the method described in patent application EP 821697 by

treatment with a periodate in an acetic medium followed by a treatment in an aqueous acid medium or a treatment with an agent capable of consuming formaldehyde in situ.

The conversion of the radical R_1 = hydroxymethyl to a formyl radical may be carried out by the action of selenium oxide by analogy with J. Korean Chem. Soc., 38(7), 537-8 (1994).

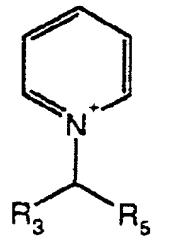
The conversion of the radical R_1 = formyl to a carboxyl radical is carried out according to the customary methods which do not adversely affect the rest of the molecule. In particular, tin oxide may be used as described in Heterocycles 32(10), 1933-40 (1991).

The conversion of the radical R_1 = carboxyl to an alkyloxycarbonyl radical is carried out according to the customary methods which do not adversely affect the rest of the molecule. In particular as described in The Chemistry of Acid Derivatives, Part I, page 411, Ed. S. Patai, John Wiley & Sons (1979).

The conversion of the radical R_1 = carboxyl to a carbamoyl radical having the structure -CO-NR'R" is carried out according to the customary methods which do not adversely affect the rest of the molecule. In particular, the corresponding amine is reacted with the acid in the presence of a condensing agent according to conventional methods of peptide chemistry:
M. Bodanszky, Principles of Peptides Synthesis,

Springer Verlag, Berlin - Heidelberg - New-York - Tokyo (1984).

According to the invention, the streptogramin derivatives of general formula (I) for which Y is a radical $=CR_3-$ and R_3 is a hydrogen atom or an alkyl radical may be prepared by the action of a pyridinium salt of general formula:



(IV)

in which R_3 is defined as above, R_5 is the residue of a ketone R_1-CO- for which R_1 is defined as above with the exception of representing a radical -NR'R", or optionally represents a protected hydroxyl radical or a nitrophenyl radical or alternatively R_5 represents the cyano radical so as to obtain a streptogramin derivative for which R_1 is an amino radical, and X^- is an anion, on the corresponding 5δ-methylene-pristinamycin of general formula (III) in which R_4 is a hydrogen atom and Ra, Rb, Rc, Rd and R_2 are defined as above optionally followed by the liberation of the hydroxyl radical or where appropriate the reduction of the nitrophenyl radical so as to obtain a derivative for which R_1 is an aminophenyl radical, or optionally followed by the action of an amine of general formula HNR'R" on the streptogramin derivative of general formula (I) for which R_1 is halomethyl, so as to obtain

the corresponding derivative for which R_1 is a radical $-CH_2NR'R''$, or followed where appropriate by the conversion of the derivative of general formula (I) for which R_1 is hydroxymethyl to a derivative for which R_1 is a radical formyl, and then where appropriate carboxyl, and then where appropriate alkyloxycarbonyl or -CONR'R" and/or optionally the mono- N-demethylation of the derivative of general formula (I) for which Rd is a dimethylamino radical to a derivative for which Rd is methylamino, and then optionally followed by the conversion to a salt, when they exist.

With no limitation being implied, the anion X^- advantageously represents a halide anion (bromide, chloride or iodide for example).

The reaction is generally carried out in the presence of an ammonium salt (ammonium acetate for example), in a solvent such as an alcohol (methanol, ethanol for example), a nitrile (acetonitrile for example), an ester (ethyl acetate for example) or a ketone (acetone for example), at a temperature of between 40°C and the reflux temperature of the reaction mixture.

When the radical R_1 contains a hydroxyl substituent, it is preferable to protect this radical beforehand according to the methods which do not adversely affect the rest of the molecule. The protection and deprotection of the hydroxyl radical is carried out according to the customary methods. For

example, the protection is carried out using an acetyl radical or using any other hydroxyl-protecting group whose introduction and removal are mentioned for example by T.W. Greene Protective Groups in Organic Synthesis, A. Wiley - Interscience Publication (1981), or by Mc Omie, Protective Groups in Organic Chemistry, Plenum Press (1973).

When it is desired to obtain a product for which R_1 is aminophenyl, it is preferable to prepare the corresponding nitrophenyl derivative and then to carry out the reduction of the nitro radical of the derivative obtained. In particular, it is possible to carry out the procedure by reduction in an acid medium (hydrochloric acid) in the presence of iron.

When it is desired to obtain the streptogramin derivative of general formula (I) for which R_1 is a radical $-CH_2NR'R"$, an amine HNR'R" is reacted with the corresponding streptogramin derivative of general formula (I) for which R_1 is halomethyl, by carrying out the procedure in the presence of a tertiary amine (triethylamine, diisopropylethylamine for example) or an excess of the amine, in an organic solvent such as an ether (tetrahydrofuran, dioxane for example), an alcohol (methanol for example), a chlorinated solvent (chloroform, dichloromethane for example), a nitrile (acetonitrile for example) or dimethyl sulphoxide at a temperature of between 40°C and the reflux temperature of the reaction mixture.

The mono-N-demethylation of the streptogramin derivative of general formula (I) for which Rd is dimethylamino may be carried out according to the method described in patent application EP 821697. The conversion of the radical R_1 = hydroxymethyl to a formyl radical may be carried out by the action of selenium oxide by analogy with J. Korean Chem. Soc., 38(7), 537-8 (1994).

The conversion of the radical R_1 = formyl to a carboxyl radical is carried out according to the customary methods which do not adversely affect the rest of the molecule. In particular, tin oxide may be used as described in Heterocycles 32(10), 1933-40 (1991).

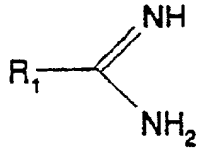
The conversion of the radical R_1 = carboxyl to an alkyloxycarbonyl radical is carried out according to the customary methods which do not adversely affect the rest of the molecule. In particular as described in The Chemistry of Acid Derivatives, Part I, page 411, Ed. S. Patai, John Wiley & Sons (1979).

The conversion of the radical R_1 = carboxyl to a carbamoyl radical having the structure -CO-NR'R" is carried out according to the customary methods which do not adversely affect the rest of the molecule. In particular, the corresponding amine is reacted with the acid in the presence of a condensing agent according to conventional methods of peptide chemistry:

M. Bodanszky, Principles of Peptides Synthesis,

Springer Verlag, Berlin - Heidelberg - New-York - Tokyo (1984).

According to the invention, the streptogramin derivatives of general formula (I) for which Y is a nitrogen atom may be prepared by the action of a salt of an amidine or of a derivative of isourea or of isothiourea of general formula:



(V)

in which R_1 is defined as for the general formula (I), with the exception of representing a radical XR^o for which X is sulphonyl or sulphinyl, or a radical NR'R" other than amino, on a streptogramin derivative of general formula (III) for which R_4 is dialkylamino, and then in order to obtain a streptogramin derivative of general formula (I) for which R_1 is a radical XR^o for which X is sulphonyl or sulphinyl, oxidation of the corresponding derivative for which X is a sulphur atom, and then in order to obtain the streptogramin derivative of general formula (I) for which R_1 is a radical NR'R", substitution of the sulphonyl derivative obtained by the action of the corresponding amine HNR'R" and/or optionally in order to obtain a derivative for which Rd is methylamino, demethylation of the derivative of general formula (I) for which Rd is a dimethylamino radical, and then optionally conversion to a salt, when they exist.

The reaction of the derivative of general formula (V) is generally carried out in an organic solvent such as an amide (dimethylformamide, dimethylacetamide for example) or a nitrile (acetonitrile for example), in the presence of a base such as in particular a tertiary amine (diisopropylethylamine, triethylamine for example) or an alkali metal bicarbonate (sodium or potassium bicarbonate for example), at a temperature of between 50 and 100°C. The reaction is advantageously carried out using the hydrochloride, the sulphate or the hydrogen sulphate of the derivative of general formula (V).

The oxidation to a sulphinyl or sulphonyl derivative is carried out respectively by treatment with 1 or 2 equivalents of Oxone° in an acid medium (for example 0.1 to 2N, preferably 0.5 to 1N sulphuric acid), at a temperature of between -60 and 60°C, in a solvent such as an alcohol (methanol, ethanol, i-propanol for example). Depending on the product prepared, it may be optionally necessary for the oxidation operation to be followed by a treatment which reduces N-oxides by any known and specific method which does not adversely affect the rest of the molecule. In particular, it is possible to carry out the procedure by heating in the presence of iron in acetic acid, or by treatment with sodium bisulphite.

The subsequent operation of substituting with

an amine may be carried out by the action of the corresponding amine of formula HNR'R", either in excess or in the presence of a base such as for example an alkali metal bicarbonate (sodium or potassium bicarbonate for example), by carrying out the procedure at a temperature of between 20 and 100°C, in an organic solvent such as an amide (dimethylformamide, dimethylacetamide for example) or a nitrile (acetonitrile for example).

The mono- N-demethylation of the streptogramin derivative of general formula (I) for which Rd is dimethylamino may be carried out according to the method described in patent application EP 821697.

The conversion of the radical R_1 = hydroxymethyl to a formyl radical may be carried out by the action of selenium oxide by analogy with J. Korean Chem. Soc., 38(7), 537-8 (1994).

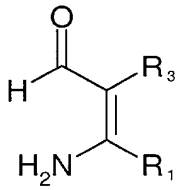
The conversion of the radical R_1 = formyl to a carboxyl radical is carried out according to the customary methods which do not adversely affect the rest of the molecule. In particular, tin oxide may be used as described in Heterocycles 32(10), 1933-40 (1991).

The conversion of the radical R_1 = carboxyl to an alkyloxycarbonyl radical is carried out according to the customary methods which do not adversely affect the rest of the molecule. In particular as described in The

Chemistry of Acid Derivatives, Part I, page 411, Ed. S. Patai, John Wiley & Sons (1979).

The conversion of the radical R_1 = carboxyl to a carbamoyl radical having the structure -CO-NR'R" is carried out according to the customary methods which do not adversely affect the rest of the molecule. In particular, the corresponding amine is reacted with the acid in the presence of a condensing agent according to conventional methods of peptide chemistry: M. Bodanszky, Principles of Peptides Synthesis, Springer Verlag, Berlin - Heidelberg - New-York - Tokyo (1984).

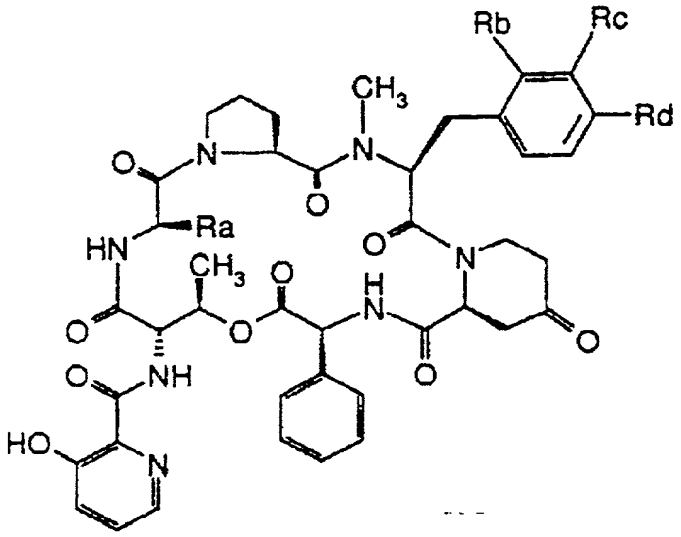
According to the invention, the streptogramin derivatives of general formula (I) for which Y is a radical $=CR_3-$, R_1 is a hydrogen atom, an alkyl, alkenyl, cycloalkyl, aromatic heterocyclyl, phenyl, substituted phenyl, halomethyl, hydroxymethyl, alkyloxymethyl, alkylthiomethyl, alkylsulphinylmethyl, alkylsulphonylmethyl or $-(CH_2)_nNR'R"$ radical, or alternatively when R_3 is a hydrogen atom, for which R_1 is formyl, carboxyl, alkoxycarbonyl or -CONR'R" as defined above and R_2 is a hydrogen atom, may also be prepared by the action of the formyl enamine of general formula:



(VI)

in which R_1 is a hydrogen atom, an alkyl, alkenyl,

cycloalkyl, aromatic heterocyclyl, phenyl, substituted phenyl, hydroxymethyl, alkyloxymethyl, alkylthiomethyl or $-(CH_2)_nNR'R"$ radical and R_3 is defined as above with the exception of representing carboxyl, on a streptogramin derivative of general formula:



in which Ra, Rb, Rc and Rd are defined as above, followed where appropriate by the conversion of the derivative for which R_3 is amide or ester to a derivative for which R_3 is carboxyl and/or followed where appropriate by the oxidation of the derivative for which R_1 is alkylthiomethyl to a derivative for which R_1 is alkylsulphinylmethyl or alkylsulphonylmethyl, or followed where appropriate by the conversion of the derivative for which R_1 is a hydroxymethyl radical to a derivative for which R_1 is halomethyl, and then where appropriate the conversion of the derivative for which R_1 is halomethyl to a derivative for which R_1 is $-CH_2NR'R"$, or followed where appropriate by the conversion of the derivative of

general formula (I) for which R_1 is hydroxymethyl to a derivative for which R_1 is a radical formyl, and then where appropriate carboxyl, alkyloxycarbonyl and/or -CONR'R", and/or optionally the mono-N-demethylation of the derivative of general formula (I) for which Rd is a dimethylamino radical to a derivative for which Rd is methylamino, and then optionally followed by conversion to a salt, when they exist.

The reaction is carried out in an organic solvent such as an alcohol (methanol, ethanol for example) at a temperature of between 20°C and the reflux temperature of the reaction mixture, in the presence of an ammonia donor such as for example ammonium acetate.

The oxidation of the alkylthiomethyl radical to an alkylsulphinylmethyl or alkylsulphonylmethyl radical is carried out under the conditions described above, by treatment with Oxone®.

The production of a streptogramin derivative of general formula (I) for which R_1 is halomethyl from a derivative for which R_1 is hydroxymethyl is carried out according to the customary methods. In particular by the action of a halogenating agent such as for example thionyl chloride.

The reaction of an amine HNR'R" on the streptogramin derivative of general formula (I) for which R_1 is halomethyl is carried out as described above.

The conversion of the radical R_1 = hydroxymethyl to a formyl radical may be carried out by the action of selenium oxide by analogy with J. Korean Chem. Soc., 38(7), 537-8 (1994).

The conversion of the radical R_1 = formyl to a carboxyl radical is carried out according to the customary methods which do not adversely affect the rest of the molecule. In particular, tin oxide may be used as described in Heterocycles 32(10), 1933-40 (1991).

The conversion of the radical R_1 = carboxyl to an alkyloxycarbonyl radical is carried out according to the customary methods which do not adversely affect the rest of the molecule. In particular as described in The Chemistry of Acid Derivatives, Part I, page 411, Ed. S. Patai, John Wiley & Sons (1979).

The conversion of the radical R_1 = carboxyl to a carbamoyl radical having the structure -CO-NR'R" is carried out according to the customary methods which do not adversely affect the rest of the molecule. In particular, the corresponding amine is reacted with the acid in the presence of a condensing agent according to conventional methods of peptide chemistry: M. Bodanszky, Principles of Peptides Synthesis, Springer Verlag, Berlin - Heidelberg - New-York - Tokyo (1984). The direct conversion of the radical R_1 = formyl to a carbamoyl radical may be carried out as described in the examples.

The mono-N-demethylation of the streptogramin derivative of general formula (I) for which Rd is dimethylamino may be carried out according to the method described in patent application EP 821697.

The enamino esters of general formula (II) are either commercially available or may be prepared according to or by analogy with the methods described in Tetrahedron Letters 38(3), 443-6(1997) and FR 2216270.

The 5δ-methylenepristinamycin derivatives of general formula (III) for which Ra is a methyl radical, or for which Ra is an ethyl radical but Rb, Rc and Rd do not simultaneously have the definitions: "Rb and Rc represent hydrogen and Rd represents hydrogen or dimethylamino", may be prepared from pristinamycin I_C, virginiamycin S4, vernamycin Bδ, pristinamycin I_B, or from their derivatives or analogues of general formula (VII) in which Ra is defined as above and the substituents Rb, Rc and Rd are either defined as in the general formula (I) in 1), with the exception of simultaneously representing Rb = Rc = hydrogen and Rd = hydrogen or dimethylamino, when Ra is ethyl, or are defined as for the general formula (I) in 2) to 7), by carrying out the procedure by analogy with the methods described in European applications EP 133097 or EP 133098 or by analogy with the methods described below in the examples.

The pyridinium salts of general formula (IV)

are prepared according to or by analogy with the method described by F. Kröhnke, Synthesis, (1976) 1-24, or according to or by analogy with the methods described below in the examples.

The amidines of formula (V) are commercially available or are prepared according to or by analogy with the method described by S. Patai, The Chemistry of amidines and Imidates, Interscience Publication, J. Wiley & Sons, Chap. 7, p. 283 (1975).

The formyl enamines of general formula (VI) may be prepared by analogy in J. Chem. Soc., Perkin trans I, 9, 2103 (1984).

The products of general formula (VII) for which Ra, Rb, Rc and Rd are defined as for the general formula (I) in 1) are natural group B streptogramins.

The preparation and separation of the components of the natural group B streptogramins is carried out by fermentation and isolation of the constituents from fermentation broth according to or by analogy with the method described by J. Preud'homme et al., Bull. Soc. Chim. Fr., vol. 2, 585 (1968) or according to Antibiotics and Chemotherapy, 5, 632 (1955).

Components of the group B streptogramins are also described in Streptogramine als Modelsysteme für den Kationentransport durch Membranen, Dissertation zur Erlangung des Doktorgrades der Mathematisch-Naturwissenschaftlichen Facultät der Georg-August

Universität zu Göttingen, Göttingen 1979, in Antibiotics III, 521 (1975) and in Antibiotics of the virginiamycin family, Inhibitors which contain synergistic components, C. Cocito, Microbiological Reviews, 145-98 (1979).

Alternatively, the preparation of the natural components of group B may be carried out by specific fermentation, as described in patent application FR 2,689,518.

The streptogramin derivatives of general formula (VII) for which Ra, Rb, Rc and Rd are defined as for the general formula (I) in 3) are prepared as described in European application EP 772630.

The streptogramin derivatives of general formula (VII) for which Ra, Rb, Rc and Rd are defined as for the general formula (I) in 4) to 7) are prepared as described in European application EP 770132.

The streptogramin derivatives of general formula (VII) for which Ra, Rb and Rc are defined as for the general formula (I) in 5) and Rd is alkylsulphinyl or alkylsulphonyl may be prepared by oxidation of the corresponding product for which Rd is alkylthio.

The streptogramin derivatives of general formula (VII) for which Ra, Rb, Rc and Rd are defined as for the general formula (I) in 2) may be prepared from pristinamycin I_B (Ra = ethyl) or from vernamycin Bδ (Ra = methyl) or from a streptogramin derivative of

general formula (I) for which Ra, Rb and Rc are defined as in 3) and Rd is $-NHCH_3$, by the action of a halogenated derivative of general formula:

$$R"'-X \qquad (VIII)$$

in which R"' is defined as for the general formula (I) in 2) and X is an iodine, bromine or chlorine atom, followed where appropriate by the chlorination or the bromination of the product obtained, when it is desired to obtain a derivative for which Rc is a chlorine or bromine atom, after starting with pristinamycin I_B or with vernamycin Bδ.

The reaction is generally carried out in an organic solvent such as an amide (dimethylformamide for example), a chlorinated solvent (chloroform, dichloromethane for example), an alcohol (methanol, ethanol for example)/chlorinated solvent mixture, a nitrile (acetonitrile for example), in dimethyl sulphoxide or N-methylpyrrolidone, at a temperature of between 20 and 100°C, optionally in the presence of sodium iodide or an alkali metal bicarbonate (sodium or potassium). Preferably, the procedure is carried out under nitrogen. It is understood that when the radical R"' contains an amino radical, it is preferable to protect this radical prior to the reaction. The protection and deprotection are carried out according to the methods indicated in the references cited above.

Where appropriate, the halogenation is advantageously carried out with an N-halosuccinimide,

in an organic solvent such as a chlorinated solvent (dichloromethane, chloroform for example) or a nitrile (acetonitrile for example), at a temperature of between 20 and 80°C.

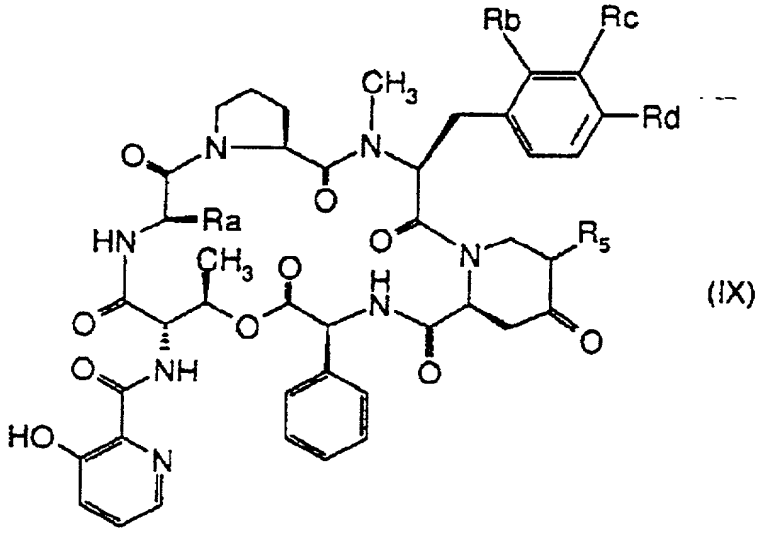
According to another alternative, the streptogramin derivatives of general formula (VII) for which Ra and Rb are defined as for the general formula (I), Rc is a hydrogen atom and Rd is a cyanomethyl methyl amino or alkyloxycarbonylmethyl methyl amino radical may also be prepared from pristinamycin I_A (Ra = ethyl) or from pristinamycin I_C (Ra = methyl) by the action of a halogenated derivative of general formula (VIII) in which R"' represents cyanomethyl or alkyloxycarbonylmethyl.

The reaction is generally carried out in an organic solvent such as an amide (dimethylformamide for example) at a temperature of between 70 and 100°C. Preferably, the procedure is carried out under nitrogen.

The streptogramin derivatives of general formula (III) for which Ra is a methyl radical and Rb, Rc and Rd are defined as in the general formula (I) or for which Ra is an ethyl radical and Rb, Rc and Rd are defined as in the general formula (I) in 2) to 7) as well as the streptogramin derivatives of general formula (VII) for which Ra, Rb, Rc and Rd are defined as for the general formula (I) in 2), except for R"' representing ethyl if Rb and Rc are hydrogen, are new

products.

All these new intermediate products can be represented by the general formula:



in which Ra is a methyl radical and Rb, Rc and Rd are defined as in the general formula (I) or Ra is an ethyl radical and Rb, Rc and Rd are defined as in the general formula (I) in 2) to 7) and R_5 represents a disubstituted methylenyl radical having the structure $=\!\!<^{R_4}_{R_2}$ for which R_2 and R_4 are defined as above, or alternatively in which Ra, Rb, Rc and Rd are defined as for the general formula (I) in 2), except for R"' representing ethyl if Rb and Rc are hydrogen, and R_5 is a hydrogen atom.

It is understood that the products of general formula (IX) are also within the scope of the present invention.

The streptogramin derivatives of general formula (I) or (IX) may be purified where appropriate

by physical methods such as crystallization or chromatography.

Some of the streptogramin derivatives of general formula (I) may be converted to the state of addition salts with acids, by known methods. It is understood that these salts, when they exist, are also included within the scope of the present invention.

As examples of addition salts with pharmaceutically acceptable acids, there may be mentioned the salts formed with inorganic acids (hydrochlorides, hydrobromides, sulphates, nitrates, phosphates) or with organic acids (succinates, fumarates, tartrates, acetates, propionates, maleates, citrates, methanesulphonates, ethanesulphonates, phenyl sulphonates, p-toluenesulphonates, isethionates, naphthylsulphonates or camphorsulphonates, or with substitution derivatives of these compounds).

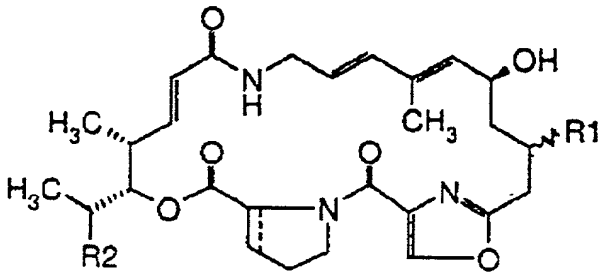
The derivatives carrying a carboxyl substituent may be converted to metal salts or to addition salts with nitrogenous bases according to methods known per se. These salts may be obtained by the action of a metal base (for example an alkali metal or alkaline-earth metal base), of ammonia or of an amine, on a product according to the invention, in an appropriate solvent such as an alcohol, an ether or water, or by an exchange reaction with a salt of an organic acid. The salt formed precipitates after optional concentration of the solution, it is separated

by filtration, decantation or freeze-drying. As examples of pharmaceutically acceptable salts, there may be mentioned the salts with the alkali metals (sodium, potassium, lithium) or with the alkaline-earth metals (magnesium, calcium), the ammonium salt, the salts of nitrogenous bases (ethanolamine, diethanolamine, trimethylamine, triethylamine, methylamine, propylamine, diisopropylamine, N,N-dimethylethanolamine, benzylamine, dicyclohexylamine, N-benzyl-β-phenethylamine, N,N'-dibenzylethylenediamine, diphenylenediamine, benzhydrylamine, quinine, choline, arginine, lysine, leucine, dibenzylamine).

The streptogramin derivatives according to the present invention have antibacterial properties and properties synergizing the antibacterial activity of the group A streptogramin derivatives. They are particularly advantageous because of their activity alone or combined with components of the group A streptogramins and especially because of their activity both by the oral and parenteral route which opens the way for an ambulatory relay treatment without modifying the nature of the medicament.

When they are combined with a component or a group A streptogramin derivative, they may in particular be chosen, depending on whether it is desired to obtain an orally or parenterally administrable form, from the natural components:

pristinamycin II_A, pristinamycin II_B, pristinamycin II_C, pristinamycin II_D, pristinamycin II_E, pristinamycin II_F, pristinamycin II_G or from the semisynthetic derivatives as described in patents or patent applications US 4,590,004 and EP 191662 or alternatively from the semisynthetic derivatives of general formula:



(α)

in which R_1 is a radical -NR'R" for which R' is a hydrogen atom or a methyl radical, R" is a hydrogen atom, an alkyl, cycloalkyl, allyl, propargyl, benzyl or -OR"' radical, R"' being a hydrogen atom, an alkyl, cycloalkyl, allyl, propargyl or benzyl radical, or $-NR_3R_4$, it being possible for R_3 and R_4 to represent a methyl radical, or to form together with the nitrogen atom to which they are attached a saturated or unsaturated 4- or 5-membered heterocycle which may in addition contain another heteroatom chosen from nitrogen, oxygen or sulphur, R_2 is a hydrogen atom or a methyl or ethyl radical, and the bond --- represents a single bond or a double bond, as well as their salts.

It is understood that the combinations of the derivatives according to the invention and of the group A streptogramins are also included within the scope of the present invention.

In vitro, combined with pristinamycin II_B, the products of general formula (I), according to the invention, have proved active at concentrations of between 0.25 and 16 mg/l on Staphylococcus aureus 209P. In vivo, on experimental infections of mice with Staphylococcus aureus IP 8203, the streptogramin derivatives of general formula (I) have proved active at doses of between 15 and 150 mg/kg orally, combined with pristinamycin II_B and between 5 and 150 mg/kg subcutaneously, combined with dalfopristin (CD_{50}), [30/70 combinations].

Finally, the products according to the invention are particularly advantageous because of the low toxicity observed in the Staphylococcus aureus IP 8203 Septicaemia model in mice. All the products, in a 30/70 combination with a group A component proved atoxic with the exception of a few of them for which a low mortality was observed at the maximum administered dose of 300 mg/kg orally or subcutaneously, in 2 administrations at an interval of 5 hours.

Some of the intermediate products defined by the general formula (IX) also exhibit antibacterial properties, especially the subgroup of streptogramin derivatives of general formula (VII). In vivo, on experimental infections of mice with Staphylococcus aureus IP 8203, they proved active orally combined with pristinamycin II_B (30/70 combinations) at doses of between 25 and 150 mg/kg.

Of particular interest are the products of general formula (I) for which

Y is a nitrogen atom or a radical $=CR_3-$,

R_1 is a hydrogen atom, a radical alkyl (1 to 8 carbons), cycloalkyl (3 to 8 carbons), heterocyclyl which is saturated or unsaturated (3 to 8 members), phenyl, phenyl which is substituted [with one or more amino, alkylamino or dialkylamino radicals] or a radical NR'R", R' and R", which are identical or different, being capable of being hydrogen atoms or alkyl radicals (1 to 3 carbons), or being capable of forming together with the nitrogen atom to which they are attached a 3- to 8-membered heterocycle optionally containing another heteroatom chosen from oxygen, sulphur or nitrogen which is optionally substituted with an alkyl radical, or alternatively when Y is a radical $=CR_3-$, R_1 may also be halomethyl, hydroxymethyl, alkylthiomethyl in which the alkyl portion is optionally substituted with NR'R", alkylsulphinylmethyl, alkylsulphonylmethyl, alkyloxymethyl, cyclopropylaminomethyl or $-(CH_2)_nNR'R"$ (n being an integer from 1 to 4 and R' and R" being defined as above), or alternatively if R_3 is a hydrogen atom, R_1 may also be formyl or -CONR'R" for which R' and R" are defined as above,

or alternatively when Y is a nitrogen atom, R_1 may also be a radical-XR° for which X is an oxygen or sulphur atom, a sulphinyl or sulphonyl radical, or an NH radical and R° is a radical alkyl (1 to 8 carbons),

heterocyclylmethyl (3 to 8 members) in which the heterocyclyl portion is attached to the methyl radical by a carbon atom, or a radical $-(CH_2)_nNR'R"$ for which R' and R" are defined as above and n is an integer from 2 to 4,

R_2 is hydrogen atom or an alkyl radical (1 to 3 carbons),

R_3 is a hydrogen atom or a carboxyl or alkyloxycarbonyl radical,

Ra is a methyl or ethyl radical, and

Rb, Rc and Rd have the definitions below:

- Rb and Rc are hydrogen atoms and Rd is a hydrogen atom or a methylamino or dimethylamino radical,
- Rb is a hydrogen atom, Rd is a radical $-NHCH_3$ or $-N(CH_3)_2$ and Rc is a chlorine or bromine atom.

And among these products, more particularly preferred are the products of general formula (I) for which

Y is a nitrogen atom or a radical $=CR_3-$,

R_1 is a hydrogen atom, a radical alkyl (1 to 3 carbons), cycloalkyl (3 to 8 carbons), heterocyclyl which is saturated or unsaturated (3 to 8 members), phenyl, phenyl which is substituted with an amino radical, or alternatively when Y is a radical $=CR_3-$, R_1 may also be acyloxymethyl,

or alternatively when Y is a nitrogen atom, R_1 may also be a radical $-XR^\circ$ for which X is an oxygen or sulphur atom or a radical NH and R° is an alkyl radical (1 to 4

carbons) or a radical $-(CH_2)_nNR'R"$ for which R' and R" which are identical or different may be hydrogen atoms or alkyl radicals (1 to 3 carbons), or form together with the nitrogen atom to which they are attached a 3- to 8-membered heterocycle optionally containing another heteroatom chosen from oxygen, sulphur or nitrogen optionally substituted with an alkyl radical, and n is an integer from 2 to 4,

R_2 is a hydrogen atom or an alkyl radical (1 to 3 carbons),

R_3 is a hydrogen atom or an alkyloxycarbonyl radical,

Ra is a methyl or ethyl radical, and

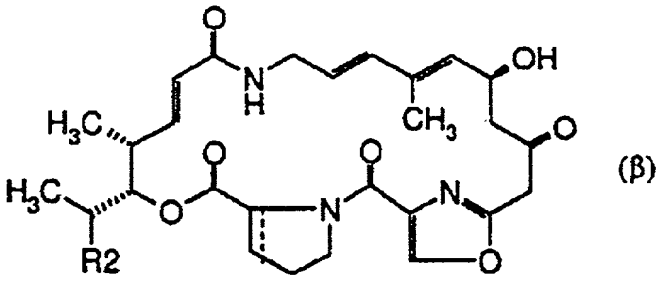
Rb, Rc and Rd have the definitions below:

- Rb and Rc are hydrogen atoms and Rd is a hydrogen atom or a methylamino or dimethylamino radical,
- Rb is a hydrogen atom, Rd is a radical $-NHCH_3$ or $-N(CH_3)_2$ and Rc is a chlorine atom.

And most particularly the following products:

- 2"-methylpyrido[2,3-5γ,5δ]pristinamycin I_E;
- 2"-cyclopropylpyrido[2,3-5γ,5δ]pristinamycin I_E;
- pyrido[2,3-5γ,5δ]pristinamycin I_E;
- 2"-ethylpyrido[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E;
- 4ε-chloro-2"-ethylpyrido[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E.

The streptogramin derivatives of general formula (α) are prepared from components of natural pristinamycin of general formula:



(β)

in which R_2 is defined as for the general formula (α), by the action of an amine of general formula:

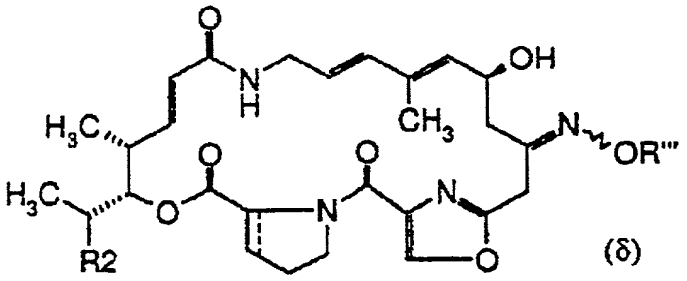
$$H_2N\text{-}R'' \qquad (\gamma)$$

in which R" is defined as for the general formula (α), followed by the action of an agent for reducing the intermediate enamine (or oxime) obtained, and then, when it is desired to obtain a streptogramin derivative of general formula (α) for which R' is a methyl radical, followed by a second reductive amination, by the action of formaldehyde or of a derivative generating formaldehyde in situ and the reduction of the intermediate enamine.

The action of the amine is carried out in an organic solvent such as an alcohol (methanol, ethanol for example), a chlorinated solvent (dichloromethane, dichloroethane, chloroform for example), a nitrile (acetonitrile for example), pyridine, at a temperature of between 0 and 30°C, and optionally in the presence of a dehydrating agent such as for example magnesium sulphate, sodium sulphate or molecular sieves. Preferably, the procedure is carried out under an inert atmosphere (argon for example). It is also possible to cause the amine salt to react.

Preferably, to prepare the derivatives for which the bond --- represents a double bond, the reaction is carried out in an organic solvent such as a nitrile (acetonitrile for example) in the presence of an acid such as an organic acid (acetic acid for example); in this case, the addition of a dehydrating agent is not necessary.

When a streptogramin derivative of general formula (α) for which R" is a radical -OR"' is prepared, it is possible to isolate the intermediate oxime of general formula:



(δ)

in which R_2 and R"' are defined as for the general formula (α), and then to reduce this product to a derivative of general formula (α) for which R' is a hydrogen atom, and optionally use it in the subsequent reductive amination operation.

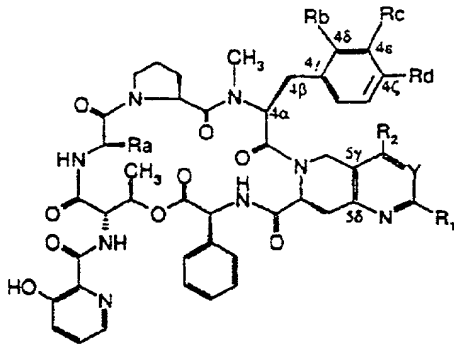
The reduction is carried out by the action of a reducing agent, for example an alkali metal borohydride (sodium cyanoborohydride or triacetoxyborohydride for example) in the presence of an organic acid (acetic acid for example) in an organic solvent as mentioned above for the amination reaction. Where appropriate, the subsequent reductive amination

operation, intended to obtain the disubstituted amine, is carried out under similar conditions.

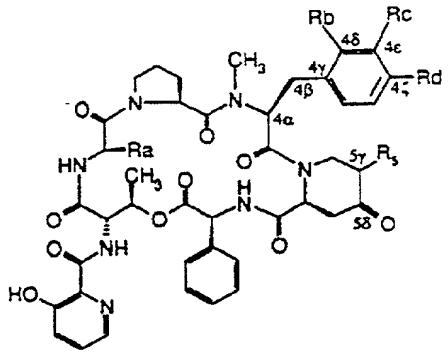
The following examples, given with no limitation being implied, illustrate the present invention.

In the text which follows, examples A to AF illustrate the preparation of the intermediate products, especially of products of general formula (IX). Examples 1 to 33 illustrate the streptogramin derivatives of general formula (I) according to the invention.

In the examples which follow, the NMR spectra were studied in deuterochloroform, the nomenclature used is that of J.O. Anteunis et al., Eur. Biochem., 58, 259 (1975) and in particular:



(I)



(IX)

The column chromatographies are performed, unless otherwise stated, at atmospheric pressure using a 0.063-0.02 mm silica. In a few specified cases, the purifications are done by flash chromatography using a 0.04-0.063 mm silica, or by high-performance liquid chromatography (HPLC) on C_8 or C_{18} graft silica.

PREPARATION OF THE DERIVATIVES OF GENERAL FORMULA (I)

Example 1

2 g of 5δ-methylenepristinamycin I_A and 0.26 g (2.3 mmol) of methyl 3-aminocrotonate are introduced into a three-necked flask containing 20 cm^3 of methanol. The mixture is refluxed for 6 hours and then an additional 0.1 g of methyl 3-aminocrotonate is added and the reflux is maintained for 1 hour. The reaction mixture is concentrated to dryness at 40°C under reduced pressure (2.7 kPa) to give 2.4 g of a yellow solid which is purified by chromatography on 30 g of silica [eluent: dichloromethane-methanol 95/5 by volume] to give a solid which is concreted from 60 cm^3 of an ether-petroleum ether mixture, filtered and then dried at 40°C under reduced pressure (90 Pa). 0.96 g of 3"-methoxycarbonyl-2"-methylpyrido[2,3-5γ,5δ]pristinamycin I_E is thus obtained in the form of a yellow solid melting at 195°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm) : 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.30 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.50 (dd, J = 16.5 and 5 Hz, 1H : 1H of CH_2 at position 5β); from 1.50 to 1.85 (mt : the 3H corresponding to the other H of CH_2 at position 3γ and to CH_2 at position 2β); 2.05 (mt, 1H : the other H of CH_2 at position 3β); 2.77 (s, 3H : $ArCH_3$); 2.85 (s, 6H : $ArN(CH_3)_2$); 2.94 (mt, 1H : 1H of CH_2 at position 4β);

3.11 (d, J = 16.5 Hz, 1H : the other H of CH_2 at position 5β); from 3.20 to 3.35 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.25 (s, 3H : NCH_3); 3.50 (mt, 1H : the other H of CH_2 at position 3δ); 3.90 (mt, 1H : 1H of CH_2 at position 5ε); 3.95 (s, 3H : $COOCH_3$); 4.61 (dd, J = 7 and 4.5 Hz, 1H : CH at position 3α); 4.80 (mt, 1H : CH at position 2α); 4.89 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.14 (dd, J = 11 and 5 Hz, 1H : CH at position 4α); 5.40 (broad d, J = 5 Hz, 1H : CH at position 5α); 5.46 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.60 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.33 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.55 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.86 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.40 (mt : the 5 aromatic H at position 6α); 7.45 (mt, 2H : 1' H_4 and 1' H_5); 7.89 (s, 1H : aromatic H at position γ with respect to N); 7.95 (broad s, 1H : 1' H_6); 8.40 (d, J = 10 Hz, 1H : CONH at position 1); 8.66 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.64 (s, 1H : OH).

Example 2

20.8 g of 5δ-methylenepristinamycin I_A, 3.94 g of ethyl 3,3-diaminoacrylate hydrochloride and 3.3 cm^3 of triethylamine are introduced into a three-necked flask containing 200 cm^3 of ethanol. The mixture is refluxed for 3 hours. After cooling, the precipitate formed is filtered, taken up in 100 cm^3 of water and the

pH adjusted to 8 with a solution of sodium bicarbonate and then the product is extracted with twice 100 cm^3 of ethyl acetate. The organic phases are combined, dried over magnesium sulphate, filtered and concentrated to dryness at 40°C under reduced pressure (2.7 kPa) to give 22 g of a yellow solid which is purified by chromatography on 500 g of silica [eluent: dichloromethane/methanol 97.5/2.5 by volume] to give a solid which is dissolved in 20 cm^3 of dichloromethane and then precipitated by addition of 60 cm^3 of diisopropyl ether. After filtration and drying at 40°C under reduced pressure (90 Pa), 1.35 g of 3"-ethoxycarbonyl-2"-aminopyrido [2,3-5γ,5δ]pristinamycin I_E are obtained in the form of a yellow solid melting at 190°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm) : 0.86 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.30 (mt, 3H : 1H of CH_2 at position 3β - 1H of CH_2 at position 3γ and 1H of CH_2 at position 5β); 1.26 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.35 (t, J = 7Hz, 3H : CH_3 of ethyl); 1.53 (mt, 1H : the other H of CH_2 at position 3γ); 1.61 and 1.70 (2 mts, 1H each : CH_2 at position 2β); 2.00 (mt, 1H : the other H of CH_2 at position 3β); from 2.75 to 2.95 (mt, 1H : the other H of CH_2 at position 5β); 2.84 (s, 6H : $ArN(CH_3)_2$); 2.90 (dd, J = 13 and 5 Hz, 1H : 1H of CH_2 at position 4β); from 3.10 to 3.25 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.20 (s, 3H :

NCH_3); 3.45 (mt, 1H : the other H of CH_2 at position 3δ); 3.74 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.30 (mt, 2H : $COOCH_2$ of ethyl); 4.55 (dd, J = 8 and 5 Hz, 1H : CH at position 3α); 4.77 (mt, 1H : CH at position 2α); 4.86 (dd, J = 10 and 1.5 Hz, 1H : CH at position 1α); 5.12 (dd, J = 11 and 5 Hz, 1H : CH at position 4α); 5.28 (2 d, respectively J = 6 Hz and J = 17 Hz, 1H each : CH at position 5α and the other H of CH_2 at position 5ε); 5.58 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.83 (dq, J = 7 and 1.5 Hz, 1H : CH at position 1β); from 6.00 to 6.50 (broad unresolved complex, 2H : $ArNH_2$); 6.36 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.61 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.84 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.15 to 7.35 (mt : the 5 aromatic H at position 6α); 7.40 (mt, 2H : 1' H_4 and 1' H_5); 7.78 (s, 1H : aromatic H at position γ with respect to N); 7.89 (broad d, J = 4 Hz, 1H : 1' H_6); 8.40 (d, J = 10 Hz, 1H : CONH at position 1); 8.60 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.61 (unresolved complex, 1H : OH).

Ethyl 3,3-diaminoacrylate hydrochloride may be prepared according to H. Meyer et al., Liebigs Ann. Chem., 1895-1908 (1977).

Example 3

By carrying out the procedure as in Example 1 but starting with 50 cm^3 of methanol, 3 g of 5δ-methylenepristinamycin I_A and 0.65 g of benzyl

3-aminocrotonate and heating under reflux for 36 hours, a precipitate is obtained, after cooling the reaction mixture to room temperature and adding 50 cm^3 of distilled water, which is filtered on sintered glass and then washed successively with 50 cm^3 of distilled water and 25 cm^3 of diisopropyl ether. The solid obtained is dissolved hot in 25 cm^3 of methanol and after cooling, the crystals formed are filtered, washed with 10 cm^3 of methanol, dried at 40°C (90 Pa) to give 1.2 g of 3"-benzyloxycarbonyl-2"-methylpyrido[2,3-5γ,5δ]pristinamycin I_E in the form of a pale-yellow solid melting at 250°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm) : 0.93 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.10 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.30 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.50 (dd, J = 17 and 5 Hz, 1H : 1H of CH_2 at position 5β); 1.58 (mt, 1H : the other H of CH_2 at position 3γ); 1.67 and 1.75 (2 mts, 1H each : CH_2 at position 2β); 2.06 (mt, 1H : the other H of CH_2 at position 3β); 2.78 (s, 3H : $ArCH_3$); 2.85 (s, 6H : $ArN(CH_3)_2$); 2.95 (mt, 1H : 1H of CH_2 at position 4β); 3.10 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5β); from 3.15 to 3.30 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.26 (s, 3H : NCH_3); 3.50 (mt, 1H : the other H of CH_2 at position 3δ); 3.90 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.62 (dd, J = 8 and 6.5 Hz, 1H : CH at position 3α);

4.81 (mt, 1H : CH at position 2α); 4.90 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.15 (dd, J = 11 and 5 Hz, 1H : CH at position 4α); 5.37 (s, 2H : $COOCH_2Ar$); 5.40 (d, J = 5 Hz, 1H : CH at position 5α); 5.45 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.61 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.33 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.58 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.87 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.50 (mt : the 12H corresponding to the 5 aromatic H at position 6α - to 1' H_4 - to 1' H_5 and to the aromatic H of benzyloxycarbonyl); 7.92 (s, 1H : aromatic H at position γ with respect to N); 7.95 (mt, 1H : 1' H_6); 8.41 (d, J = 10 Hz, 1H : CONH at position 1); 8.68 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.66 (s, 1H : OH).

1.95 g of 3"-benzyloxycarbonyl-2"-methyl-pyrido[2,3-5γ,5δ]pristinamycin I_E and then 1.6 g of 20% palladium hydroxide on carbon and 2 cm^3 of 1,4-cyclohexadiene are introduced under a nitrogen stream into a three-necked flask containing 50 cm^3 of methanol. The mixture is heated at 60°C for 30 minutes and then cooled to room temperature. The catalyst is filtered on Whatman filter paper and the filtrate concentrated at 45°C under reduced pressure (2.7 kPa) so as to obtain a final volume of 5 cm^3. 100 cm^3 of diisopropylether are then added and the precipitate formed is filtered,

washed with 25 cm^3 of diisopropylether and then dried at 40°C under reduced pressure (90 Pa) to give 0.95 g of 3"-carboxy-2"-methylpyrido[2,3-5γ,5δ]pristinamycin I_E in the form of a cream-coloured solid melting at 234°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm) : 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.35 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.32 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.39 (mt, 1H : 1H of CH_2 at position 5β); 1.60 (mt, 1H : the other H of CH_2 at position 3γ); 1.71 and 1.80 (2 mts, 1H each : CH_2 at position 2β); 2.05 (mt, 1H : 1H of CH_2 at position 3β); 2.67 (s, 3H : $ArCH_3$); 2.78 (s, 6H : $ArN(CH_3)_2$); 2.92 (mt, 1H : 1H of CH_2 at position 4β); 3.05 (very broad d, J = 16 Hz, 1H : the other H of CH_2 at position 5β); from 3.15 to 3.35 (mt, 1H : the other H of CH_2 at position 4β); 3.25 (s, 3H : NCH_3); 3.48 (mt, 1H : 1H of CH_2 at position 3δ); 3.57 (mt, 1H : the other H of CH_2 at position 3δ); 4.01 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.60 (mt, 1H : CH at position 3α); 4.88 (mt, 1H : CH at position 2α); 4.94 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.12 (mt, 1H : CH at position 4α); 5.40 (unresolved complex, 1H : CH at position 5α); 5.43 (d, HzJ = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.69 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.29 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.85 (d, J = 8 Hz, 2H : aromatic H at position 4δ); 7.13 (broad d, 1H : CONH at position 2);

from 7.20 to 7.45 (mt : the 7H corresponding to the 5 aromatic H at position 6α - to 1' H_4 and to 1' H_5); 7.79 (broad s, 1H : aromatic H at position γ with respect to N); 7.92 (broad s, 1H : 1' H_6); 8.34 (d, J = 10 Hz, 1H : CONH at position 1); 8.65 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.61 (s, 1H : OH).

Benzyl 3-aminocrotonate may be prepared as described by J. Daxoll, J. Chem. Soc., 3802-3808 (1953).

Example 4

By carrying out the procedure as in Example 1 but starting with 150 cm^3 of methanol, 20 g of 5δ-methylenepristinamycin I_B and 0.26 g of methyl 3-aminocrotonate and after refluxing for 6 hours, 20 g of a yellow product are obtained, which product is purified by two successive chromatographies on 1 kg and 200 g of silica respectively [eluent: dichloromethane/methanol 98/2 by volume] to give after drying at 40°C, under reduced pressure (90 Pa), 13.4 g of 3"-methoxycarbonyl-2"-methylpyrido [2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E in the form of a yellow solid melting at 208°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm) : 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.35 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.29 (d, J = 7 Hz, 3H : CH_3 at position 1γ); from 1.55 to 1.80 (mt : the 3H corresponding to the other H of CH_2 at position 3γ and to CH_2 at position

2β); 1.57 (dd, J = 16 and 5.5 Hz, 1H : 1H of CH_2 at position 5β); 2.03 (mt, 1H : the other H of CH_2 at position 3β); 2.67 (s, 3H : $ArCH_3$); 2.76 (s, 6H : $ArNCH_3$); 2.91 (dd, J = 13 and 5 Hz, 1H : 1H of CH_2 at position 4β); from 3.10 to 3.30 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.13 (d, J = 16 Hz, 1H : the other H of CH_2 at position 5β); 3.22 (s, 3H :NCH_3); 3.49 (mt, 1H : the other H of CH_2 at position 3δ); 3.88 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 3.92 (s, 3H : $COOCH_3$); 4.60 (dd, J = 8 and 5.5 Hz, 1H : CH at position 3α); 4.78 (mt, 1H : CH at position 2α); 4.87 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.12 (dd, J = 11 at position 5 Hz, 1H : CH at position 4α); 5.38 (d, J = 5.5 Hz, 1H : CH at position 5α); 5.44 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.61 (d, J = 8.5 Hz, 1H : CH at 6α); 5.87 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.18 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.52 (broad d, 1H : CONH at position 2); 6.79 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.15 to 7.35 (mt : the 5 aromatic H at position 6α); 7.42 (mt, 2H : 1' H_4 and 1' H_5); 7.88 (s, 1H : aromatic H at position γ with respect to N); 7.92 (mt, 1H : 1' H_6); 8.39 (d, J = 10 Hz, 1H : CONH at position 1); 8.64 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.62 (s, 1H : OH).

Example 5

3.4 g of 5δ-methylenepristinamycin I_A, 1 g of

3,3-dimethyl-2-oxo-1-butylpyridinium bromide and then 3 g of ammonium acetate are introduced into a three-necked flask containing 100 cm^3 of methanol. The mixture is refluxed for 3 hours and then concentrated to dryness at 40°C under reduced pressure (2.7 kPa). 100 cm^3 of distilled water are then added and then the mixture is extracted with twice 100 cm^3 of ethyl acetate. The organic phases are decanted off, combined, dried over sodium sulphate, filtered and then concentrated to dryness at 40°C under reduced pressure (2.7 kPa) to give 3.6 g of an orange-coloured solid which is purified by two successive chromatographies on 40 g of silica (eluent: dichloromethane/methanol 95/5 by volume) to give a product which is taken up in 60 cm^3 of an ether-petroleum ether mixture. After filtration and drying at 40°C under reduced pressure (90 Pa), 0.64 g of 2"-tert-butylpyrido[2,3-5γ,5δ]pristinamycin I_E is obtained in the form Hzof a cream-coloured solid melting at 196°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm) : 0.91 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.32 (s, 9H : $ArC(CH_3)_3$); 1.60 (mt, 1H : the other H of CH_2 at position 3γ); 1.66 and 1.75 (2 mts : the 2H corresponding to CH_2 at position 2β); 1.98 (dd, J = 16 and 5.5 Hz, 1H : 1H of CH_2 at position 5β); 2.02 (mt, 1H : the other H of CH_2 at position 3β); 2.86 (s, 6H :

$ArN(CH_3)_2$); 3.01 (dd, J = 14 and 6.5 Hz, 1H : 1H of CH_2 at position 4β); from 3.10 to 3.40 (mt, 3H : the other H of CH_2 at position 4β - the other H of CH_2 at position 5β and 1H of CH_2 at position 3δ); 3.18 (s, 3H : NCH_3); 3.51 (mt, 1H : the other H of CH_2 at position 3δ); 3.94 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.58 (t, J = 7.5 Hz, 1H : CH at position 3α); 4.81 (mt, 1H : CH at position 2α); 4.90 (broad d, J = 10 Hz, 1H : CH at position 1α); from 5.35 to 5.50 (mt, 3H : CH at position 4α - the other H of CH_2 at position 5ε and CH at position 5α); 5.65 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.43 (d, J = 8 Hz, 2H : aromatic H at 4ε); 6.75 (d, J = 10 Hz, 1H : CONH at position 2); 6.87 (d, J = 8 Hz, 2H : aromatic H at position 4δ); 7.12 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); from 7.25 to 7.45 (mt : the 8H corresponding to the 5 aromatic H at position 6α - to the aromatic H at position γ with respect to N - to 1' H_4 and to 1' H_5); 7.87 (mt, 1H : 1' H_6); 8.49 (d, J = 10 Hz, 1H : CONH at position 1); 8.73 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.70 (s, 1H : OH).

3,3-dimethyl-2-oxo-1-butylpyridinium bromide may be prepared as described by F. Kroencke, Chem. Ber., 69, 921-923 (1936).

Example 6

404 g of 5δ-methylenepristinamycin I_A, 78.8 g of 1-acetonylpyridinium chloride and then 354 g of

ammonium acetate are introduced into a three-necked flask containing 2 litres of acetone. The mixture is refluxed for 1 hour and then concentrated to dryness at 40°C under reduced pressure (2.7 kPa). 10 litres of distilled water are then added and then the mixture is extracted with 500 cm^3 of dichloromethane and then with 3 litres of ethyl acetate. The organic phases are decanted off, combined, dried over sodium sulphate, filtered and then concentrated to dryness at 40°C under reduced pressure (2.7 kPa) to give 205 g of an orange-coloured solid which is purified by chromatography on 1 kg of silica (eluent: dichloromethane/methanol 98/2 by volume) to give 64.7 g of a product which is taken up in 60 cm^3 of diisopropyl ether and then recrystallized twice from 100 cm^3 of methanol. After filtration and drying at 40°C under reduced pressure (90 Pa), 23.3 g of a product which is 2"-methylpyrido [2,3-5γ,5δ]pristinamycin I_E are obtained in the form of a yellow solid melting at 253°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm) : 0.94 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.35 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.59 (mt, 1H : the other H of CH_2 at position 3γ); from 1.60 to 1.85 (mt: the 2H corresponding to CH_2 at position 2β); 1.69 (dd, J = 16 and 6 Hz, 1H : 1H of CH_2 at position 5β); 2.06 (mt, 1H : the other H of CH_2 at position 3β); 2.48 (s, 3H : $ArCH_3$); 2.86 (s, 6H :

$ArN(CH_3)_2$); 2.98 (dd, J = 13.5 and 5.5 Hz, 1H : 1H of CH_2 at position 4β); 3.15 (d, J = 16 Hz, 1H : the other H of CH_2 at position 5β); from 3.15 to 3.30 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.24 (s, 3H : NCH_3); 3.50 (mt, 1H : the other H of CH_2 at position 3δ); 3.92 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.61 (dd, J = 8 and 5.5 Hz, 1H : CH at position 3α); 4.81 (mt, 1H : CH at position 2α); 4.90 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.23 (dd, J = 10 and 5.5 Hz, 1H : CH at position 4α); 5.42 (d and broad d respectively, J = 17 Hz and J = 5.5 Hz, 1H each : the other H of CH_2 at position 5e and CH at position 5α); 5.63 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.90 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.36 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.61 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.87 (d, J = 8 Hz, 2H : aromatic H at 4δ); 6.96 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); from 7.20 to 7.40 (mt : the 5 aromatic H at position 6α); 7.34 (d, J = 8 Hz, 1H : aromatic H at position γ with respect to N); 7.41 (limiting AB, 2H : 1' H_4 and 1' H_5); 7.92 (mt, 1H : 1' H_6); 8.44 (d, J = 10 Hz, 1H : CONH at position 1); 8.65 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.66 (s, 1H : OH).

1-acetonylpyridinium chloride may be prepared according to H. Dreser, Arch. Pharm., 232, 183 (1894).

Example 7

By carrying out the procedure as in Example 6

but starting with 50 g of 5δ-methylenepristinamycin I_A in 1 litre of acetone, 13.7 g of 1-(2-oxobutyl)-pyridinium bromide, 44 g of ammonium acetate and heating for 1 hour under reflux and then adding 2.6 g of 1-(2-oxobutyl)pyridinium bromide and refluxing for an additional one hour, 19.5 g of a product are obtained after purification by chromatography on 200 g of silica (eluent: dichloromethane/methanol 97/3 by volume), which product can be purified by crystallization in the following manner. 8 g of this solid are dissolved hot in a mixture of 30 cm^3 of methanol and 1 cm^3 of distilled water. After cooling, the crystals obtained are collected to give 3.9 g of a solid which is recrystallized under similar conditions. After filtration and drying at 40°C under reduced pressure (90 Pa), 1.7 g of 2"-ethylpyrido[2,3-5γ,5δ]-pristinamycin I_E are obtained in the form of a white solid melting at 263°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.89 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.35 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.22 (t, J = 7.5 Hz, 3H : CH_3 of ethyl); 1.28 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.53 (mt, 1H : the other H of CH_2 at position 3γ); from 1.60 to 1.80 (mt: the 2H corresponding to CH_2 at position 2β); 1.76 (dd, J = 16 and 5.5 Hz, 1H : 1H of CH_2 at position 5β); 2.00 (mt, 1H : the other H of CH_2 at position 3β); 2.72 (q, J = 7.5 Hz, 2H: $ArCH_2$ of

ethyl); 2.82 (s, 6H: $ArN(CH_3)_2$); 2.94 (dd, J = 13.5 and 5.5 Hz, 1H : 1H of CH_2 at position 4β); from 3.10 to 3.25 (mt, 3H : the other H of CH_2 at position 4β - the other H of CH_2 at position 5β and 1H of CH_2 at position 3β); 3.18 (s, 3H : NCH_3); 3.46 (mt, 1H : the other H of CH_2 at position 3β); 3.90 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.57 (dd, J = 8 and 5.5 Hz, 1H : CH at position 3α); 4.75 (mt, 1H : CH at position 2α); 4.84 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.21 (dd, J = 9 and 5.5 Hz, 1H : CH at position 4α); 5.38 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.39 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.60 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.85 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.32 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.53 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.82 (d, J = 8 Hz, 2H : aromatic H at position 4δ); 6.93 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); from 7.25 to 7.40 (mt: the 5 aromatic H at position 6α); 7.29 (d, J = 8 Hz, 1H : the aromatic H at position γ with respect to N); 7.33 (mt, 2H : 1' H_4 and 1' H_5); 7.85 (mt, 1H : 1' H_6); 8.39 (d, J = 10 Hz, 1H : CONH at position 1); 8.63 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.62 (s, 1H: OH).

1-(2-Oxobutyl)pyridinium bromide may be prepared by analogy with 1-(2-oxobutyl)pyridinium iodide as described by R.P. Soni, J.P. Saxena, J. Indian Chem. Soc. 58, 885-887 (1981).

15 g of 1-bromo-2-butanone and 40 cm^3 of pyridine are introduced into a three-necked flask containing 150 cm^3 of ethanol and the mixture is heated for 2 hours under reflux. After concentrating to dryness at 40°C under reduced pressure (2.7 kPa), the residue is taken up in 100 cm^3 of diethyl ether. After filtration, washing with twice 70 cm^3 of diethyl ether, the precipitate is dried to give 22 g of a yellow solid melting at 181°C.

^1H NMR spectrum (250 MHz, $(CD_3)_2SO$ d6, δ in ppm): 1.06 (t, J = 7 Hz, 3H : CH_3 of ethyl); 2.70 (q, J = 7 Hz, 2H : $COCH_2$ of ethyl); 5.83 (s, 2H : NCH_2CO); 8.25 (dd, J = 8 and 5 Hz, 2H : aromatic H at position β of pyridine); 8.69 (t, J = 8 Hz, 2H : aromatic H at position γ of pyridine); 8.91 (d, J = 5 Hz, 2H : aromatic H at position α of pyridine).

Example 8

By carrying out the procedure as in Example 5 but starting with 9.8 g of 5δ-methylenepristinamycin I_A in 500 cm^3 of methanol, 2.7 g of 1-cyclopropylcarbonyl-methylpyridinium bromide, 8.6 g of ammonium acetate and heating for 40 minutes under reflux, 1.1 g of product are obtained after purification by chromatography on 150 g of silica (eluent: dichloromethane/methanol 97/3 by volume), which product may be recrystallized from 11 cm^3 of boiling methanol. After cooling, the crystals obtained are filtered and then rinsed with 5 cm^3 of methanol to give 0.47 g of 2"-cyclopropylpyrido-

[2,3-5γ,5δ]pristinamycin I_E in the form of white crystals melting at 198°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): from 0.80 to 1.00 (mt, 4H : the 2 CH_2 of cyclopropyl); 0.91 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.35 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.30 (d, J = 7 Hz, 3H : CH_3 at position 1γ); from 1.55 to 1.80 (mt : the 2H corresponding to CH_2 at position 2β); 1.57 (mt, 1H : the other H of CH_2 at position 3γ); 1.68 (dd, J = 16 and 6.5 Hz, 1H : 1H of CH_2 at position 5β); 1.96 (mt, 1H : $ArCH_2$ of cyclopropyl); 2.04 (mt, 1H : the other H of CH_2 at position 3β); 2.86 (s, 6H: $ArN(CH_3)_2$); 2.96 (dd, J = 13 and 6 Hz, 1H : 1H of CH_2 at position 4β); 3.10 (d, J = 16 Hz, 1H : the other H of CH_2 at position 5β); from 3.10 to 3.30 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.22 (s, 3H : NCH_3); 3.49 (mt, 1H : the other H of CH_2 at position 3β); 3.90 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.60 (dd, J = 8 and 6 Hz, 1H : CH at position 3α); 4.79 (mt, 1H : CH at position 2α); 4.88 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.23 (dd, J = 10 and 6 Hz, 1H : CH at position 4α); 5.36 (broad d, J = 6.5 Hz, 1H : CH at position 5α); 5.38 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.62 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.34 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.58 (d, J = 9.5 Hz, 1H : CONH at

position 2); from 6.75 to 6.90 (mt, 3H : aromatic H at position 4δ and aromatic H at position β with respect to N); 7.08 (d, J = 8 Hz, 1H : aromatic H at position γ with respect to N); from 7.20 to 7.35 (mt : the 5 aromatic H at position 6α); 7.40 (limiting AB, 2H : 1' H_4 and 1' H_5); 7.91 (mt, 1H : 1' H_6); 8.43 (d, J = 10 Hz, 1H : CONH at position 1); 8.63 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.62 (s, 1H: OH).

1-Cyclopropylcarbonylmethylpyridinium bromide may be prepared in the following manner:

2.4 g of 1-bromomethylcyclopropylketone and 5.8 cm^3 of pyridine are introduced into a three-necked flask containing 40 cm^3 of ethanol and then the mixture is heated for 2 hours under reflux. After concentrating to dryness at 40°C under reduced pressure (2.7 kPa), the residue is taken up in twice 30 cm^3 of diethyl ether. After filtration, washing with diethyl ether, the precipitate is dried under reduced pressure (90 Pa) to give 3.4 g of 1-cyclopropylcarbonylmethylpyridinium bromide in the form of a cream-coloured solid melting at 160°C.

^1H NMR spectrum (300 MHz, $(CD_3)_2SO$ d6, δ in ppm): 1.08 and 1.16 (2 mts, 2H each : the 2 CH_2 of cyclopropane); 2.34 (mt, 1H : COCH of cyclopropane); 6.06 (s, 2H : NCH_2CO); 8.24 (dd, J = 8 and 5 Hz, 2H : aromatic H at position β of pyridine); 8.70 (t, J = 8 Hz, 2H : aromatic H at position γ of pyridine);

8.96 (d, J = 5 Hz, 2H : aromatic H at position α of pyridine).

Bromomethylcyclopropylketone may be prepared according to V.K. Jinaraj et al., Ind. J. Chem., Sect. B, 22, 841-45 (1983).

Example 9

By carrying out the procedure as in Example 5 but starting with 10 g of 5δ-methylenepristinamycin I_A in 300 cm^3 of methanol, 2.2 g of 1-cyanomethylpyridinium bromide, 8.5 g of ammonium acetate and heating for 3 hours under reflux, a product is obtained after purification by chromatography on 70 g of silica (eluent: dichloromethane/methanol 90/10 by volume), which product is repurified 3 times by the same method, changing the nature of the eluent (dichloromethane/methanol 95/5, and then dichloromethane/methanol 97/3 and then dichloromethane/methanol 95/5) to give 0.16 g of 2"-aminopyrido[2,3-5γ,5δ]pristinamycin I_E in the form of a white solid melting at 222°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.90 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.35 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.28 (d, J = 7 Hz, 3H : CH_3 at position 1γ); from 1.45 to 1.80 (mt, the 4H corresponding to the other H of CH_2 at position 3γ - to 1H of CH_2 at position 5β and to CH_2 at position 2β); 2.01 (mt, 1H : the other H of CH_2 at position 3β); from 2.80 to 3.00 (mt, 2H : the other H of CH_2 at position 5β and 1H of CH_2 at

position 4β); 2.89 (s, 6H : $ArN(CH_3)_2$); from 3.10 to 3.25 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.20 (s, 3H : NCH_3); 3.45 (mt, 1H : the other H of CH_2 at position 3δ); 3.80 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.27 (unresolved complex, 2H : $ArNH_2$); 4.57 (dd, J = 8.5 and 5.5 Hz, 1H : CH at position 3α); 4.76 (mt, 1H : CH at position 2α); 4.86 (dd, J = 10 and 1.5 Hz, 1H : CH at position 1α); 5.18 (dd, J = 10 and 6 Hz, 1H : CH at position 4α); 5.27 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.32 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.60 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.86 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.30 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); 6.37 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.54 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.83 (d, J = 8 Hz, 2H : aromatic H at position 4δ); 7.09 (d, J = 8 Hz, 1H : aromatic H at position γ with respect to N); from 7.15 to 7.40 (mt : the 7H corresponding to the 5 aromatic H at position 6α - to 1' H_4 and to 1' H_5); 7.84 (dd, J = 4 and 1.5 Hz, 1H : 1' H_6); 8.38 (d, J = 10 Hz, 1H : CONH at position 1); 8.55 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.61 (s, 1H: OH).

Example 10

By carrying out the procedure as in Example 5 but starting with 30 g of 5δ-methylenepristinamycin I_A in 300 cm^3 of methanol, 7.1 g of 1-(3-chloro-

2-oxopropyl)pyridinium chloride (at 50%), 26 g of ammonium acetate and heating for 10 minutes under reflux, 1.4 g of a product are obtained after 2 successive chromatographies on 400 g of silica (eluent: dichloromethane/methanol 98/2 by volume), which product is purified by HPLC on 10 µm C_8 silica (eluent: water:acetonitrile:70/30 by volume containing 0.1% trifluoroacetic acid). The fractions are combined, the acetonitrile removed at 40°C under reduced pressure (2.7 kPa) and the aqueous phase adjusted to pH 7 with 3 cm^3 of water saturated with sodium bicarbonate. The aqueous phase is washed with twice 60 cm^3 of dichloromethane. The organic phases are pooled, dried over sodium sulphate, filtered and then concentrated to dryness under reduced pressure (2.7 kPa) to give 0.4 g of a yellow solid which is concreted from 60 cm^3 of a diethyl ether/petroleum ether mixture, filtered and then dried under reduced pressure (90 Pa). 0.3 g of 2"-chloromethylpyrido[2,3-5γ,5δ]pristinamycin I_E is thus obtained in the form of a cream-coloured solid melting at 194°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.35 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.30 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.57 (mt, 1H : the other H of CH_2 at position 3γ); from 1.60 to 1.80 (mt : the 2H corresponding to CH_2 at position 2β); 1.63 (dd, J = 16 and 6 Hz, 1H : 1H of CH_2

at position 5β); 2.03 (mt, 1H : the other H of CH_2 at position 3β); 2.85 (s, 6H : $ArN(CH_3)_2$); 2.95 (dd, J = 13 and 5.5 Hz, 1H : 1H of CH_2 at position 4β); 3.12 (d, J = 16 Hz, 1H : the other H of CH_2 at position 5β); from 3.15 to 3.30 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.23 (s, 3H : NCH_3); 3.49 (mt, 1H : the other H of CH_2 at position 3δ); 3.93 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.58 (limiting AB, J = 14 Hz, 2H : $ArCH_2Cl$); from 4.55 to 4.75 (mt, 1H : CH at position 3α); 4.79 (mt, 1H : CH at position 2α); 4.88 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.18 (dd, J = 10.5 and 5.5 Hz, 1H : CH at position 4α); 5.40 (broad d, J = 6 Hz, 1H : CH at position 5α); 5.46 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.60 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.87 (broad q, J = 7 Hz: 1H : CH at position 1β); 6.36 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.55 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.86 (d, J = 8 Hz, 2H : aromatic H at position 4δ); 7.22 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); from 7.25 to 7.40 (mt : the 5 aromatic H at position 6α); 7.38 (d, J = 8 Hz, 1H : aromatic H at position γ with respect to N); 7.42 (mt, 2H : 1' H_4 and 1' H_5); 7.89 (mt, 1H : 1' H_6); 8.40 (d, J = 10 Hz, 1H : CONH at position 1); 8.68 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.64 (s, 1H: OH).

1-(3-Chloro-2-oxopropyl)pyridinium chloride

may be prepared in the following manner:

66.9 g of 1,3-dichloroacetone chloride are introduced into a three-necked flask containing 800 cm^3 of diethyl ether. 28 cm^3 of pyridine are added dropwise and the mixture is kept stirring overnight. The precipitate obtained is filtered, washed with twice 100 cm^3 of diethyl ether and then dried at 40°C under 90 Pa to give 29.2 g of 1-(3-chloro-2-oxopropyl)-pyridinium chloride in the form of a cream-coloured solid melting at 92°C and which is used as it is.

Example 11

By carrying out the procedure as in Example 6 but starting with 36.5 g of 5δ-methylenepristinamycin I_A in 350 cm^3 of methanol, 9.6 g of 1-(3-acetoxy-2-oxopropyl)pyridinium chloride, 32.2 g of ammonium acetate and heating for 40 minutes under reflux, a solid is obtained which is chromatographed on 350 g of silica (eluent: dichloromethane/methanol gradient 100/0 then 99/1 then 98/2 then 96/4 by volume) to give 1.3 g of a yellow solid. The latter is purified by HPLC on 10 μm C_8 silica (eluent: water/acetonitrile 70/30 by volume, containing 0.1% trifluoroacetic acid). The fractions are combined, the acetonitrile removed at 40°C under reduced pressure (2.7 kPa) and the pH of the aqueous phase adjusted to 7 by addition of water saturated with sodium bicarbonate. The aqueous phase is extracted with 3 times 200 cm^3 of dichloromethane. The organic phases are pooled, dried over magnesium

sulphate, filtered and concentrated at 40°C under reduced pressure (2.7 kPa to give 0.5 g of 2"-hydroxymethylpyrido[2,3-5γ,5δ]pristinamycin I_E in the form of a white solid melting at 190°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.35 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.50 (dd, J = 16 and 6 Hz, 1H : 1H of CH_2 at position 5β); from 1.50 to 1.70 (mt : the 2H corresponding to 1H of CH_2 at position 2β and the other H of CH_2 at position 3γ); 1.75 (mt, 1H : the other H of CH_2 at position 2β); 2.05 (mt, 1H : the other H of CH_2 at position 3β); 2.82 (s, 6H : $ArN(CH_3)_2$); 2.93 (dd, J = 12 and 5 Hz, 1H : 1H of CH_2 at position 4β); 3.11 (d, J = 16 Hz, 1H : the other H of CH_2 at position 5β); from 3.15 to 3.30 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.25 (s, 3H : NCH_3); 3.48 (mt, 1H : the other H of CH_2 at position 3δ); 3.91 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 3.94 (unresolved complex, 1H : OH); 4.61 (dd, J = 8 and 5.5 Hz, 1H : CH at position 3α); 4.67 Hz(broad s, 2H : $ArCH_2O$); 4.80 (mt, 1H : CH at position 2α); 4.89 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.14 (dd, J = 12 and 5 Hz, 1H : CH at position 4α); 5.37 (broad d, J = 6 Hz, 1H : CH at position 5α); 5.44 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.60 (d, J = 8.5 Hz, 1H :

Example 12

By carrying out the procedure as in Example 5 but starting with 6 g of 5δ-methylenepristinamycin I_A in 100 cm^3 of methanol, 1.9 g of 1-phenacylpyridinium bromide, 5.3 g of ammonium acetate and heating for 30 minutes under reflux, a solid is obtained after purification by chromatography on 90 g of silica [eluent: dichloromethane/methanol 95/5 by volume] which is taken up in 60 cm^3 of an ether-petroleum ether mixture. After filtration and drying at 40°C under reduced pressure (90 Pa), 0.8 g of 2"-phenylpyrido-[2,3-5γ,5δ]pristinamycin I_E is obtained in the form of a yellow solid melting at 212°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.93 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.32 (d, J = 7 Hz, 3H : CH_3 at position 1γ); from 1.50 to 1.85 (mt : the 4H corresponding to 1H of CH_2 at position 5β) - to the other H of CH_2 at position 3γ and to CH_2 at position 2β); 2.06 (mt, 1H : the other 1H of CH_2 at position 3β); 2.70 (s, 6H : $ArN(CH_3)_2$); 2.98 (dd, J = 13 and 5.5 Hz, 1H : 1H of CH_2 at position 4β); from 3.15 to 3.35 (mt, 3H : the other H of CH_2 at position 5β - the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.26 (s, 3H : NCH_3); 3.50 (mt, 1H : the other H of CH_2 at position 3δ); 4.00 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.64 (dd, J = 8 and 5.5 Hz, 1H : CH at position 3α); 4.82 (mt, 1H

: CH at position 2α); 4.89 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.23 (dd, J = 11 and 5.5 Hz, 1H : CH at position 4α); 5.46 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.50 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.66 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.90 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.34 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.60 (d, J = 10 Hz, 1H : CONH at position 2); 6.88 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.25 to 7.50 (mt: the 11H corresponding to the 5 aromatic H at position 6α - to the aromatic H at position γ with respect to N - to the aromatic H at the para position of the phenyl - to the aromatic H at the meta position of the phenyl - to 1' H_4 and to 1' H_5); 7.56 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); 8.00 (mt, 3H : 1' H_6 and aromatic H at the ortho position of the phenyl); 8.45 (d, J = 10 Hz, 1H : CONH at position 1); 8.58 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.66 (s, 1H: OH).

1-Phenacylpyridinium bromide may be prepared according to F. Kroencke and H. Timmler, Chem. Ber., 69, 614 (1936).

Example 13

By carrying out the procedure as in Example 5 but starting with 29.6 g of 5δ-methylenepristinamycin I_A in 200 cm^3 of methanol, 10.9 g of 1-(4-nitrophenacyl)-pyridinium bromide and 26 g of ammonium acetate and heating for 40 minutes under reflux, a solid is

obtained after purification by chromatography on 500 g of silica [eluent: dichloromethane/methanol 95/5 by volume] which is taken up in 60 cm^3 of an ether-petroleum ether mixture. After filtration and drying at 40°C under reduced pressure (90 Pa), 16 g of 2"-(4-nitrophenyl)pyrido[2,3-5γ,5δ]pristinamycin I_E are obtained in the form of an orange-coloured solid melting at 345°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.94 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); from 1.55 to 1.85 (mt : the 4H corresponding to the other H of CH_2 at position 3γ - to 1H of CH_2 at position 5β and to CH_2 at position 2β); 2.08 (mt, 1H : the other H of CH_2 at position 3β); 2.68 (s, 6H : $ArN(CH_3)_2$); 2.96 (dd, J = 13 and 5 Hz, 1H : 1H of CH_2 at position 4β); from 3.15 to 3.35 (mt, 3H : the other H of CH_2 at position 5β - the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.26 (s, 3H : NCH_3); 3.61 (mt, 1H : the other H of CH_2 at position 3δ); 3.99 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.64 (dd, J = 7 and 6 Hz, 1H : CH at position 3α); 4.81 (mt, 1H : CH at position 2α); 4.90 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.17 (dd, J = 11.5 and 5 Hz, 1H : CH at position 4α); 5.44 (broad d, J = 5 Hz, 1H : CH at position 5α); 5.53 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.63 (d, J = 8.5 Hz, 1H : CH at

position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.32 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.58 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.88 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.40 (mt : the 5 aromatic H at position 6α); from 7.45 to 7.55 (mt, 2H : 1' H_4 and 1' H_5); 7.49 (d, J = 8 Hz, 1H : aromatic H at position γ with respect to N); 7.64 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); 7.90 (broad d, J = 4 Hz, 1H : 1' H_6); 8.20 and 8.31 (2 d, J = 8.5 Hz, 2H each : respectively the aromatic H at the meta position with respect to the NO_2 and the aromatic H at the ortho position with respect to the NO_2); 8.42 (d, J = 10 Hz, 1H : CONH at position 1); 8.70 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.66 (s, 1H: OH).

9.1 g of 2"-(4-nitrophenyl)pyrido[2,3-5γ,5δ]-pristinamycin I_E and then 50 g of iron powder and 1 cm^3 of concentrated hydrochloric acid are introduced into a three-necked flask containing 90 cm^3 of ethanol and 20 cm^3 of distilled water and then the mixture is refluxed for 30 minutes. The insoluble matter is removed by filtration, washed with 60 cm^3 of ethanol and then the filtrate is concentrated to dryness at 40°C under reduced pressure (2.7 kPa). The residue obtained is taken up in 300 cm^3 of water, the pH adjusted to 8 by addition of sodium bicarbonate and the aqueous phase extracted with twice 100 cm^3 of dichloromethane. After

drying over sodium sulphate, filtration and concentration to dryness under reduced pressure, 11.5 g of a chestnut-coloured solid are obtained, which solid is purified by chromatography on 120 g of silica [eluent: dichloromethane/methanol 95/5 by volume]. The solid obtained is concreted from 60 cm^3 of an ether-petroleum ether mixture, filtered and dried at 40°C under reduced pressure (90 Pa) to give 1.5 g of 2"-(4-aminophenyl)pyrido[2,3-5γ,5δ]pristinamycin I_E in the form of a yellow solid melting at 226°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.93 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.30 (d, J = 7 Hz, 3H : CH_3 at position 1γ); from 1.50 to 1.85 (mt : the 4H corresponding to the other H of CH_2 at position 3γ - to 1H of CH_2 at position 5β and to CH_2 at position 2β); 2.04 (mt, 1H : the other H of CH_2 at position 3β); 2.73 (s, 6H : $ArN(CH_3)_2$); 2.96 (dd, J = 13 and 4.5 Hz, 1H : 1H of CH_2 at position 4β); from 3.15 to 3.35 (mt, 3H : the other H of CH_2 at position 5β - the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.24 (s, 3H : NCH_3); 3.50 (mt, 1H : the other H of CH_2 at position 3δ); 3.80 (unresolved complex, 2H : NH_2); 3.97 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.63 (mt, 1H : CH at position 3α); 4.81 (mt, 1H : CH at position 2α); 4.90 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.21 (dd, J = 10 and 4.5 Hz, 1H : CH at position 4α); 5.42 (mt, 1H : CH

at position 5α); 5.45 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.64 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.89 (mt, 1H : CH at position 1β); 6.33 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.58 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.74 (d, J = 8 Hz, 2H : aromatic H at the ortho position with respect to the NH_2); 6.88 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.50 (mt : the 9H corresponding to the 5 aromatic H at position 6α - to 1' H_4 - to 1' H_5 - to the aromatic H at position γ with respect to N and to the aromatic H at position β with respect to N); 7.82 (d, J = 8 Hz, 2H : aromatic H at the meta position with respect to NH_2); 7.98 (unresolved complex, 1H : 1' H_6); 8.44 (d, J = 10 Hz, 1H : CONH at position 1); 8.64 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.66 (s, 1H: OH).

Example 14

By carrying out the procedure as in Example 5 but starting with 10 g of 5δ-methylenepristinamycin I_A in 100 cm^3 of methanol, 4 g of 1-(4-diethylamino-phenacyl)pyridinium bromide and 9 g of ammonium acetate and heating for 40 minutes under reflux, a solid is obtained after purification by chromatography on 150 g of silica [eluent: dichloromethane/methanol 95/5 by volume] which is taken up in 60 cm^3 of an ether-petroleum ether mixture. After filtration and drying at 40°C under reduced pressure (90 Pa), 2.4 g of 2"-(4-diethylaminophenyl)pyrido[2,3-5γ,5δ]pristinamycin

I_E are obtained in the form of a yellow solid melting at 210°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.93 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.22 (t, J = 7 Hz, 6H : the 2 CH_3 of diethylamino); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.58 (mt : 1H : the other H of CH_2 at position 3γ); from 1.60 to 1.85 (mt: the 3H corresponding to 1H of CH_2 at position 5β and to CH_2 at position 2β); 2.05 (mt, 1H : the other H of CH_2 at position 3β); 2.75 (s, 6H : $ArN(CH_3)_2$); 2.98 (dd, J = 13 and 5.5 Hz, 1H : 1H of CH_2 at position 4β); from 3.15 to 3.35 (mt, 3H : the other H of CH_2 at position 5β - the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.24 (s, 3H : NCH_3); 3.42 (mt, 4H : the 2 NCH_2 of diethylamino); 3.50 (mt, 1H : the other H of CH_2 at position 3δ); 3.97 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.62 (dd, J = 8 and 5.5 Hz, 1H : CH at position 3α); 4.81 (mt, 1H : CH at position 2α); 4.90 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.24 (dd, J = 10 and 5.5 Hz, 1H : CH at position 4α); 5.43 (2 d, respectively J = 6 Hz and J = 17 Hz, 2H : CH at position 5α and the other H of CH_2 at position 5ε); 5.66 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.89 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.34 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.60 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.72 (d, J = 8 Hz, 2H : aromatic H at the

ortho position with respect to diethylamino); 6.87 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.40 (mt : the 6H corresponding to the 5 aromatic H at position 6α and to the aromatic H at position γ with respect to N); from 7.40 to 7.50 (mt, 3H : 1' H_4 - 1' H_5 and aromatic H at position β with respect to N); 7.85 (d, J = 8 Hz, 2H : aromatic H at the meta position with respect to diethylamino); 7.98 (mt, 1H : 1' H_6); 8.44 (d, J = 10 Hz, 1H : CONH at position 1); 8.63 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.67 (s, 1H: OH).

1-(4-Diethylaminophenacyl)pyridinium bromide may be prepared in the following manner:

10 g of 4-diethylaminophenacyl bromide are introduced into a three-necked flask containing 200 cm^3 of tetrahydrofuran and then 15 cm^3 of pyridine are added dropwise. The stirring is continued for 90 hours and then the precipitate formed is filtered and then washed with 60 cm^3 of diethyl ether. After drying at 40°C under reduced pressure (90 Pa), 14.1 g of 4-diethylamino-phenylpyridinium bromide are obtained in the form of a white solid melting at > 260°C.

^1H NMR spectrum (300 MHz, $(CD_3)_2SO$ d6, δ in ppm): 1.18 (t, J = 7 Hz, 6H : the 2 CH_3 of diethylamino); 3.50 (q, J = 7 Hz, 4H : the 2 NCH_2 of diethylamino); 6.39 (s, 2H : NCH_2COAr); 6.84 (d, J = 8 Hz, 2H : aromatic H at the ortho position with respect to diethylamino); 7.88 (d, J = 8 Hz, 2H :

aromatic H at the meta position with respect to diethylamino); 8.28 (dd, J = 8 and 5 Hz, 2H : aromatic H at position β of pyridine); 8.74 (t, J = 8 Hz, 2H : aromatic H at position γ of pyridine); 9.02 (d, J = 5 Hz, 2H : aromatic H at position α of pyridine).

Example 15

By carrying out the procedure as in Example 5 but starting with 5 g of 5δ-methylenepristinamycin I_A in 75 cm^3 of methanol, 2.05 g of 1-[2-oxo-2-(2-pyridyl)-ethyl]pyridinium bromide hydrobromide and 4.3 g of ammonium acetate and heating for 3 hours under reflux, a solid is obtained which is purified by preparative HPLC on 400 g of 10 µm Kromasil® C_8 silica [eluent: water/acetonitrile 70/30 by volume containing 0.1% trifluoroacetic acid]. After concentrating the fractions in order to remove the acetonitrile, the aqueous phase is neutralized to pH 7-8 with a 10% solution of sodium bicarbonate. The precipitate obtained during the neutralization is filtered, taken up in 25 cm^3 of dry dichloromethane and then the organic phase dried over sodium sulphate, filtered and concentrated to dryness under reduced pressure to give a solid which is taken up in 10 cm^3 of diisopropyl ether. After filtration and drying at 40°C under reduced pressure (90 Pa), 0.94 g of 2"-(2-pyridyl)pyrido[2,3-5γ,5δ]pristinamycin I_E is obtained in the form of a beige solid 1.38 g melting at 190°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.93 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.32 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.58 (mt : 1H : the other H of CH_2 at position 3γ) ; from 1.60 to 1.85 (mt: the 2H corresponding to CH_2 at position 2β); 1.66 (dd, J = 16 and 5 Hz, 1H : 1H of CH_2 at position 5β); 2.07 (mt, 1H : the other H of CH_2 at position 3β); 2.65 (s, 6H : $ArN(CH_3)_2$); 2.96 (dd, J = 13 and 5.5 Hz, 1H : 1H of CH_2 at position 4β); from 3.15 to 3.35 (mt, 3H : the other H of CH_2 at position 4β - the other H of CH_2 at position 5β and 1H of CH_2 at position 3δ); 3.26 (s, 3H : NCH_3); 3.51 (mt, 1H : the other H of CH_2 at position 3δ); 4.00 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.64 (dd, J = 8 and 6.5 Hz, 1H : CH at position 3α); 4.82 (mt, 1H : CH at position 2α); 4.91 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.19 (dd, J = 12 and 5.5 Hz, 1H : CH at position 4α); 5.44 (broad d, J = 5 Hz, 1H : CH at position 5α); 5.52 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.66 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.90 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.31 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.58 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.88 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.25 to 7.40 (mt : the 6H corresponding to the 5 aromatic H at position 6α and to H_5 of pyridine); from 7.40 to 7.55 (mt, 3H : aromatic H at position γ with respect to N -

1' H_5 and 1' H_4); 7.78 (split t, J = 8 and 1.5 Hz, 1H : H_4 of pyridine); 8.02 (broad d, J = 4 Hz, 1H : 1' H_6); 8.23 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); 8.42 (mt, 2H : H_3 of pyridine and CONH at position 1); 8.66 (d, J = 8.5 Hz, 1H : CONH at position 6); 8.68 (broad mt, 1H : H_6 of pyridine); 11.67 (s, 1H: OH).

1-[2-Oxo-2-(2-pyridyl)ethyl]pyridinium bromide hydrobromide may be prepared by analogy with F. Krönhke et al., Synthesis, 1-24 (1976):

5 g of 2-bromoacetylpyridine hydrobromide and 7 cm^3 of pyridine are introduced into a three-necked flask containing 50 cm^3 of tetrahydrofuran. The stirring is maintained for 2 days at room temperature and then the precipitate formed is filtered, washed with 30 cm^3 of tetrahydrofuran and then dried at 40°C under reduced pressure (90 Pa) to give 6.9 g of 1-[2-oxo-2-(2-pyridyl)ethyl]pyridinium hydrobromide in the form of a beige solid which is used as it is.

2-Bromoacetylpyridine hydrobromide may be prepared as described by J.L. Garcia Ruano et al., Tetrahedron, 43, 4407-4416 (1987).

Example 16

5 g of 5δ-methylenepristinamycin I_A, 2.1 g of 1-[2-oxo-2-(3-pyridyl)ethyl]pyridinium hydrobromide and 4.4 g of ammonium acetate are introduced into a three-necked flask containing 75 cm^3 of methanol. After refluxing for 1 hour, the reaction mixture is

concentrated by half and then poured over 200 cm^3 of distilled water. The orange precipitate which appeared is filtered to give 3.5 g of a solid which is purified by chromatography on 50 g of silica [eluent: dichloromethane/methanol 97/3]. After concentrating the fractions, 1 g of a yellow solid is obtained which is crystallized from 30 cm^3 of methanol. 0.4 g of 2"-(3-pyridyl)pyrido[2,3-5γ,5δ]pristinamycin I_E is obtained after filtration and drying at 40°C under reduced pressure (90 Pa) in the form of a white solid melting at 265°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.58 (mt, 1H : the other H of CH_2 at position 3γ); from 1.50 to 1.85 (mt : the 3H corresponding to CH_2 at position 2β and to 1H of CH_2 at position 5β); 2.05 (mt, 1H : the other H of CH_2 at position 3β); 2.68 (s, 6H : $ArN(CH_3)_2$); 2.95 (dd, J = 13 and 5.5 Hz, 1H : 1H of CH_2 at position 4β); from 3.20 to 3.35 (mt, 3H : the other H of CH_2 at position 4β - the other H of CH_2 at position 5β and 1H of CH_2 at position 3δ); 3.26 (s, 3H : NCH_3); 3.49 (mt, 1H : the other H of CH_2 at position 3δ); 3.98 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.61 (dd, J = 8 and 6 Hz, 1H : CH at position 3α); 4.80 (mt, 1H : CH at position 2α); 4.89 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.17 (dd, J = 12 and 5.5 Hz, 1H : CH

at position 4α); 5.43 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.49 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.63 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.30 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.55 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.86 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.25 to 7.40 (mt : the 6H corresponding to the 5 aromatic H at position 6α - to H_5 of pyridine); from 7.40 to 7.55 (mt, 3H : aromatic H at position γ with respect to N - 1' H_5 and 1' H_4); 7.58 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); 8.00 (dd, J = 4 and 1.5 Hz, 1H : 1' H_6); 8.31 (dt, J = 8 and 1.5 Hz, 1H : H_4 of pyridine); 8.40 (d, J = 10 Hz, 1H : CONH at position 1); 8.63 (dd, J = 5 and 1.5 Hz, 1H : H_6 of pyridine); 8.67 (d, J = 8.5 Hz, 1H : CONH at position 6); 9.20 (d, J = 1.5 Hz, 1H : H_2 of pyridine); 11.64 (s, 1H: OH).

1-[2-Oxo-2-(3-pyridyl)ethyl]pyridinium hydrobromide may be prepared according to F. Krönhke, Synthesis, 1-24 (1976).

Example 17

2 g of 2"-ethylpyrido[2,3-5γ,5δ]-pristinamycin I_E, 0.17 cm^3 of ethylene glycol, 2.2 cm^3 of acetic acid and 0.44 g of tetra-n-butylammonium periodate are introduced into a three-necked flask containing 30 cm^3 of dichloromethane. The mixture is stirred for 18 hours at room temperature and then

washed with 3 times 20 cm^3 of water. The organic phase is decanted off, dried over magnesium sulphate, filtered and concentrated at 45°C under reduced pressure (2.7 kPa). The residue obtained is taken up in 50 cm^3 of water and 10 cm^3 of 0.5 N sulphuric acid and stirred for 5 minutes. The insoluble matter is removed by filtration and the aqueous phase extracted with 3 times 30 cm^3 of ethyl acetate. The aqueous phase is adjusted to about pH 8 with a saturated solution of sodium bicarbonate and then extracted with 3 times 30 cm^3 of dichloromethane. The chloromethylene phases are pooled, dried over sodium sulphate, filtered and concentrated to dryness under reduced pressure to give 1.7 g of a beige foam which is purified by chromatography on 50 g of silica [eluent: dichloromethane/methanol 97/3 by volume]. 0.4 g of 2"-ethylpyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E is thus obtained after drying at 40°C under 90 Pa in the form of a cream-coloured solid melting at 194°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.93 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.27 (t, J = 7.5 Hz, 3H : CH_3 of ethyl); 1.32 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.59 (mt, 1H : the other H of CH_2 at position 3γ); from 1.60 to 1.85 (mt : the 2H corresponding to CH_2 at position 2β); 1.81 (dd, J = 16 and 5.5 Hz, 1H : 1H of

CH_2 at position 5β); 2.06 (mt, 1H : the other H of CH_2 at position 3β); 2.72 (s, 3H : $ArNCH_3$); 2.77 (q, J = 7.5 Hz, 2H : $ArCH_2$ of ethyl); 2.97 (dd, J = 13.5 and 5.5 Hz, 1H : 1H of CH_2 at position 4β); from 3.15 to 3.30 (mt, 3H : the other H of CH_2 at position 4β - the other H of CH_2 at position 5β and 1H of CH_2 at position 3δ); 3.22 (s, 3H : NCH_3); 3.51 (mt, 1H : the other H of CH_2 at position 3δ); 3.67 (unresolved complex, 1H : ArNH); 3.93 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.61 (dd, J = 8 and 6 Hz, 1H : CH at position 3α); 4.81 (mt, 1H : CH at position 2α); 4.90 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.26 (dd, J = 10 and 5.5 Hz, 1H : CH at position 4α); 5.42 (broad d and d respectively, J = 5.5 Hz and J = 17 Hz, 1H each : CH at position 5α and the other H of CH_2 at position 5ε); 5.65 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.90 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.24 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.60 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.82 (d, J = 8 Hz, 2H : aromatic H at position 4δ); 6.99 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); from 7.25 to 7.40 (mt : the 5 aromatic H at position 6α); 7.33 (d, J = 8 Hz, 1H : aromatic H at position γ with respect to N); 7.40 (limiting AB, 2H : 1' H_4 and 1' H_5); 7.92 (mt, 1H : 1' H_6); 8.47 (d, J = 10 Hz, 1H : CONH at position 1); 8.69 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.67 (s, 1H: OH).

Example 18

By carrying out the procedure as in Example 5 but starting with 10 g of 5δ-methylenepristinamycin I_B in 150 cm^3 of methanol, 4.1 g of 1-[2-oxo-2-(2-pyridyl)-ethyl]pyridinium hydrobromide and 8.7 g of ammonium acetate and heating for 3 hours under reflux, 7.5 g of a solid are obtained, which solid is purified by preparative HPLC on 400 g of 10 µm Kromasil® C_8 silica [eluent: water-acetonitrile 70/30 by volume containing 0.1% trifluoroacetic acid]. After concentrating the fractions in order to remove the acetonitrile, the aqueous phase is neutralized to pH 7-8 with a 10% solution of sodium bicarbonate. The precipitate obtained during the neutralization is filtered, taken up in 50 cm^3 of dry dichloromethane and then the organic phase dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure to give a solid which is taken up in 50 cm^3 of diisopropyl ether. After filtration and drying at 40°C under reduced pressure (90 Pa), 1.12 g of 2"-(2-pyridyl)pyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E are obtained in the form of a pink solid melting at 200°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.93 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.32 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.58 (mt : 1H : the other H of CH_2 at position 3γ);

from 1.60 to 1.85 (mt, 2H : CH_2 at position 2β); 1.70 (dd, J = 16 and 5.5 Hz, 1H : 1H of CH_2 at position 5β); 2.06 (mt, 1H : the other H of CH_2 at position 3β); 2.53 (s, 3H : $ArNCH_3$); 2.94 (dd, J = 13 and 5.5 Hz, 1H : 1H of CH_2 at position 4β); from 3.15 to 3.30 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.25 (s, 3H : NCH_3); 3.29 (d, J = 16 Hz, 1H : the other H of CH_2 at position 5β); 3.50 (mt, 1H : the other H of CH_2 at position 3δ); 3.99 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.62 (dd, J = 8 and 6 Hz, 1H : CH at position 3α); 4.81 (mt, 1H : CH at position 2α); 4.90 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.16 (dd, J = 10.5 and 5.5 Hz, 1H : CH at position 4α); 5.43 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.52 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.67 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.90 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.15 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.58 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.81 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.25 to 7.40 (mt : the 6H corresponding to the 5 aromatic H at position 6α and to H_5 of pyridine); from 7.40 to 7.55 (mt, 3H : aromatic H at position γ with respect to N - 1' H_5 and 1' H_4); 7.78 (split t, J = 8 and 1.5 Hz, 1H : H_4 of pyridine); 8.01 (broad d, J = 4 Hz, 1H : 1' H_6); 8.20 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); 8.38 (d, J = 8 Hz, 1H : H_3 with respect to pyridine); 8.46 (d, J = 10 Hz, 1H : CONH at position 1); 8.66 (d,

J = 8.5 Hz, 1H : CONH at position 6); 8.70 (broad d, J = 4 Hz, 1H : H_6 of pyridine); 11.68 (s, 1H: OH).

1-[2-Oxo-2-(2-pyridyl)ethyl]pyridinium hydrobromide may be prepared according to F. Krönhke et al., Synthesis, 1-24 (1976).

Example 19

15 g of 2"-methylpyrido[2,3-5γ,5δ]-pristinamycin I_E, 1.25 cm^3 of ethylene glycol, 16.4 cm^3 of acetic acid and 3.33 g of tetra-n-butylammonium periodate are introduced into a three-necked flask containing 60 cm^3 of methylene chloride. The mixture is stirred for 10 hours at room temperature and then the reaction mixture is washed with twice 50 cm^3 of distilled water. The organic phase is decanted off and then concentrated to dryness at 40°C under reduced pressure (2.7 kPa). The residue is taken up in 100 cm^3 of water and 200 cm^3 of 0.5 N sulphuric acid and then washed with 5 times 100 cm^3 of ethyl acetate. The aqueous phase is decanted off, adjusted to pH 7-8 with 200 cm^3 of a saturated sodium bicarbonate solution and then extracted with twice 150 cm^3 of ethyl acetate. The organic phase is dried over magnesium sulphate and then concentrated to dryness (40°C-2.7 kPa) to give 32 g of a solid which is chromatographed on 1 kg of silica [eluent: dichloromethane/methanol gradient 99/1 to 97.5/2.5]. After concentration to dryness of the fractions and then crystallization from ethyl acetate, 4.7 g of 2"-methylpyrido[2,3-5γ,5δ]-

(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E are obtained after drying at 40°C under reduced pressure (90 Pa) in the form of white crystals melting at 244°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.57 (mt : 1H : the other H of CH_2 at position 3γ); from 1.60 to 1.85 (mt, 2H : CH_2 at position 2β); 1.73 (dd, J = 16 and 6.5 Hz, 1H : 1H of CH_2 at position 5β); 2.05 (mt, 1H : the other H of CH_2 at position 3β); 2.49 (s, 3H : $ArCH_3$); 2.69 (s, 3H : $ArNCH_3$); 2.95 (dd, J = 13.5 and 5.5 Hz, 1H : 1H of CH_2 at position 4β); from 3.15 to 3.30 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.16 (d, J = 16 Hz, 1H : the other H of CH_2 at position 5β); 3.22 (s, 3H : NCH_3); 3.49 (mt, 1H : the other H of CH_2 at position 3β); 3.68 (unresolved complex, 1H : ArNH); 3.91 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.60 (dd, J = 8 and 5.5 Hz, 1H : CH at position 3α); 4.79 (mt, 1H : CH at position 2α); 4.88 (dd, J = 10 and 1.5 Hz, 1H : CH at position 1α); 5.21 (dd, J = 10 and 5.5 Hz, 1H : CH at position 4α); 5.40 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.41 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.63 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.88 (dq, J = 7 and 1.5 Hz, 1H : CH at position 1β); 6.23 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.58 (d, J = 9.5 Hz,

1H : CONH at position 2); 6.81 (d, J = 8 Hz, 2H : aromatic H at position 4δ); 6.96 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); from 7.20 to 7.40 (mt : the 5 aromatic H at position 6α); 7.33 (d, J = 8 Hz, 1H : aromatic H at position γ with respect to N); 7.40 (limiting AB, 2H : 1' H_4 and 1' H_5); 7.91 (mt, 1H : 1' H_6); 8.44 (d, J = 10 Hz, 1H : CONH at position 1); 8.65 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.65 (s, 1H: OH).

Example 20

1.7 g of 2"-chloromethylpyrido[2,3-5γ,5δ]-pristinamycin I_E and 0.6 cm^3 of morpholine are added successively to a three-necked flask containing 30 cm^3 of tetrahydrofuran and then the mixture is refluxed. After 18 hours, an additional 0.3 cm^3 of morpholine is added and 0.3 cm^3 of triethylamine and then the reflux is maintained for 6 hours. The reaction mixture is then concentrated to dryness under reduced pressure at 40°C at 2.7 kPa. The residue obtained is taken up in twice 50 cm^3 of water and then the aqueous phase is extracted with twice 50 cm^3 of dichloromethane. The organic phases are combined, dried over sodium sulphate, filtered and then concentrated to dryness to give 1.3 g of product which is purified by chromatography on 80 g of silica [eluent: dichloromethane/methanol gradient from 98/2 to 97.3 by volume] to give 0.3 g of a solid which is concreted in a mixture with 0.26 g of the same product obtained from another test, from 60 cm^3 of an ether-

petroleum ether mixture (20/80 by volume). After filtration and drying at 40°C under reduced pressure (90 Pa), 0.3 g of 2"-(N-morpholinomethyl)pyrido-[2,3-5γ,5δ]pristinamycin I_E is obtained in the form of a yellow solid melting at 189°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.29 (d, J = 7 Hz, 3H : CH_3 at position 1γ); from 1.50 to 1.70 (mt, the 2H corresponding to the other H of CH_2 at position 3γ and to 1H of CH_2 at position 2β); 1.75 (mt, 1H : the other H of CH_2 at position 2β); 1.87 (dd, J = 16 and 6 Hz, 1H : 1H of CH_2 at position 5β); 2.03 (mt, 1H : the other H of CH_2 at position 3β); 2.50 (mt, 4H : the 2 NCH_2 of morpholine); 2.87 (s, 6H : $ArN(CH_3)_2$); 2.98 (dd, J = 13.5 and 6 Hz, 1H : 1H of CH_2 at position 4β); from 3.10 to 3.35 (mt, 3H : the other H of CH_2 at position 5β - the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.22 (s, 3H : NCH_3); 3.50 (mt, 1H : the other H of CH_2 at position 3δ); 3.59 (s, 2H : $ArCH_2N$); 3.74 (mt, 4H : the 2 OCH_2 of morpholine); 3.94 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.60 (dd, J = 8 and 5 Hz, 1H : CH at position 3α); 4.79 (mt, 1H : CH at position 2α); 4.88 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.29 (dd, J = 9 and 6 Hz, 1H : CH at position 4α); 5.43 (mt, 1H : CH at position 5α); 5.45 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε) 5.63 (d, J = 8.5 Hz, 1H :

CH at position 6α); 5.90 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.36 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.58 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.85 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.45 (mt : the 9H corresponding to the 5 aromatic H at position 6α - to the aromatic H at position β with respect to N - to the aromatic H at position γ with respect to N - to 1' H_5 and 1' H_4); 7.84 (broad d, J = 4 Hz, 1H : 1' H_6); 8.43 (d, J = 10 Hz, 1H : CONH at position 1); 8.70 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.66 (s, 1H : OH).

2"-Chloromethylpyrido[2,3-5γ,5δ]pristinamycin I_E may be obtained as described in Example 10.

Example 21

By carrying out the procedure as in Example 20 but starting with 50 cm^3 of tetrahydrofuran, 3.2 g of 2"-chloromethylpyrido[2,3-5γ,5δ]-pristinamycin I_E and 1.1 cm^3 of N-methylpiperazine, 2.3 g of a solid are obtained after refluxing for 2 hours, which solid is purified by two successive chromatographies on 100 g of silica [eluent: dichloromethane/methanol 95/5 by volume] to give 0.4 g of 2"-(4-methyl-1-piperazinylmethyl)pyrido[2,3-5γ,5δ]-pristinamycin I_E in the form of a yellow solid melting at 221°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.93 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20

to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ) ; from 1.50 to 1.85 (mt : the 4H corresponding to the other H of CH_2 at position 3γ - to CH_2 at position 2β and to 1H of CH_2 at position 5β); 2.03 (mt, 1H : the other H of CH_2 at position 3β); 2.32 (s, 3H : NCH_3 of piperazine); from 2.40 to 2.70 (mt, 8H : the 4 NCH_2 of piperazine); 2.90 (s, 6H : $ArN(CH_3)_2$); 2.99 (dd, J = 13.5 and 6 Hz, 1H : 1H of CH_2 at position 4β); from 3.15 to 3.35 (mt, 3H : the other H of CH_2 at position 5β - the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.22 (s, 3H : NCH_3); 3.50 (mt, 1H : the other H of CH_2 at position 3δ); 3.62 (s, 2H : $ArCH_2N$); 3.95 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.60 (dd, J = 7.5 and 5.5 Hz, 1H : CH at position 3α); 4.80 (mt, 1H : CH at position 2α); 4.89 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.28 (dd, J = 9 and 6 Hz, 1H : CH at position 4α); 5.51 (mt, 1H : CH at position 5α); 5.55 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.65 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.89 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.37 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.59 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.86 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.45 (mt : the 9H corresponding to the 5 aromatic H at position 6α - to the aromatic H at position β with respect to N - to the aromatic H at position γ with respect to N - to 1' H_5 and 1' H_4); 7.87 (broad d,

J = 4 Hz, 1H : 1' H_6); 8.43 (d, J = 10 Hz, 1H : CONH at position 1); 8.70 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.64 (unresolved complex, 1H: OH).

Example 22

4.6 g of 5δ-dimethylaminomethylene-pristinamycin I_A, 1.1 g of O-methylisourea hydrogen sulphate and 1.75 g of sodium bicarbonate are introduced into a three-necked flask containing 30 cm^3 of dimethylformamide. The mixture is heated at 65°C for 18 hours. After cooling, 100 cm^3 of distilled water are added and the product is extracted with 3 times 100 cm^3 of ethyl acetate. The organic phases are combined, washed with 200 cm^3 of brine, dried over magnesium sulphate, filtered and concentrated to dryness at 40°C under reduced pressure (2.7 kPa) to give 5.05 g of a yellow oil which is purified by chromatography on 90 g of silica [eluent: dichloromethane/methanol 97/3 by volume] to give 1.2 g of a solid. The solid obtained is purified by HPLC on 450 g of 10 µm C_8 silica (eluent: phosphate buffer pH 2.9/acetonitrile: 60/40 by volume). The fractions are combined, the acetonitrile removed at 40°C under reduced pressure (2.7 kPa) and the aqueous phase adjusted to pH 7 with water saturated with sodium bicarbonate and then extracted with dichloromethane. The organic phase is decanted off, dried over magnesium sulphate, filtered and concentrated at 40°C under reduced pressure (2.7 kPa) to give a solid which is triturated in 10 cm^3 of diisopropyl ether. After

filtration and drying at 40°C (90 Pa), 0.40 g of 2"-methoxypyrimido[4,5-5γ,5δ]pristinamycin I_E is obtained in the form of a white solid melting at 195-198°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.91 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.35 (mt, 3H : 1H of CH_2 at position 3β - 1H of CH_2 at position 3γ and 1H of CH_2 at position 5β); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.58 (mt, 1H : the other H of CH_2 at position 3γ); from 1.60 to 1.85 (mt, the 2H corresponding to CH_2 at position 2β); 2.05 (mt, 1H : the other H of CH_2 at position 3β); 2.85 (s, 6H : $ArN(CH_3)_2$); 2.91 (dd, J = 12 and 4.5 Hz, 1H : 1H of CH_2 at position 4β); 2.93 (d, J = 16.5 Hz, 1H : the other H of CH_2 at position 5β); from 3.15 to 3.30 (mt, 1H : 1H of CH_2 at position 3δ); 3.21 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 3.25 (s, 3H : NCH_3); 3.50 (mt, 1H : the other H of CH_2 at position 3δ); 3.76 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 3.95 (s, 3H : $ArOCH_3$); 4.61 (dd, J = 8 and 5.5 Hz, 1H : CH at position 3α); 4.80 (mt, 1H : CH at position 2α); 4.88 (dd, J = 10 and 1.5 Hz, 1H : CH at position 1α); 5.07 (dd, J = 12 and 4.5 Hz, 1H : CH at position 4α); 5.33 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.41 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.64 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.88 (split q, J = 7 and 1.5 Hz, 1H : CH at position 1β); 6.33 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.51 (d,

J = 10 Hz, 1H : CONH at position 2); 6.85 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.40 (mt : the 5 aromatic H at position 6α); 7.44 (dd, J = 8.5 and 1.5 Hz, 1H : 1' H_4); 7.49 (dd, J = 8.5 and 4 Hz, 1H : 1' H_5); 7.94 (dd, J = 4 and 1.5 Hz, 1H : 1' H_6); 8.16 (s, 1H : CH=N); 8.37 (d, J = 10 Hz, 1H : CONH at position 1); 8.69 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.63 (s, 1H: OH).

Example 23

By carrying out the procedure as in Example 22 but starting with 12 cm^3 of dimethylformamide, 2.76 g of 5δ-dimethylaminomethylene-pristinamycin I_A, 0.54 g of S-methylisothiouronium sulphate and 0.35 g of sodium bicarbonate and after 4 hours at 65°C, 2.5 g of a yellow solid are obtained after cooling, addition of 100 cm^3 of ethyl acetate to the reaction mixture, washing of the organic phase with 3 times 80 cm^3 of water, decantation of the organic phase which is dried over magnesium sulphate, filtered and concentrated to dryness at 40°C under reduced pressure (2.7 kPa). The solid is chromatographed on 200 g of silica [eluent: dichloromethane/methanol 95/5 by volume] to give 1.9 g of a solid which is purified by HPLC on 450 g of 10 µm C_8 silica [eluent: water-acetonitrile 35-65 by volume containing 0.1% trifluoroacetic acid]. The fractions are combined, the acetonitrile removed at 40°C under reduced pressure (2.7 kPa) and the aqueous phase adjusted to pH 7-8 with

water saturated with sodium bicarbonate. The white precipitate formed is filtered, washed with twice 5 cm^3 of diisopropyl ether and dried at 40°C under 90 Pa to give 0.7 g of 2"-methylthiopyrimido[4,5-5γ,5δ]-pristinamycin I_E in the form of a cream-coloured solid melting at 197°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.91 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.40 (mt, 3H : 1H of CH_2 at position 3β - 1H of CH_2 at position 3γ and 1H of CH_2 at position 5β); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.59 (mt, 1H : the other H of CH_2 at position 3γ); 1.67 and 1.76 (2 mts, 1H each : CH_2 at position 2β); 2.06 (mt, 1H : the other H of CH_2 at position 3β); 2.52 (s, 3H : $ArSCH_3$); from 2.80 to 3.00 (mt, 2H : 1H of CH_2 at position 4β and the other H of CH_2 at position 5β); 2.88 (s, 6H : $ArN(CH_3)_2$); from 3.15 to 3.35 (mt, 2H : 1H of CH_2 at position 3δ and the other H of CH_2 at position 4β); 3.26 (s, 3H : NCH_3); 3.50 (mt, 1H : the other H of CH_2 at position 3δ); 3.77 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.61 (dd, J = 8 and 5.5 Hz, 1H : CH at position 3α); 4.80 (mt, 1H : CH at position 2α); 4.89 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.06 (dd, J = 12 and 4.5 Hz, 1H : CH at position 4α); 5.32 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.41 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.65 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.35 (d, J = 8 Hz, 2H : aromatic H at

position 4ε); 6.52 (d, J = 10 Hz, 1H : CONH at position 2); 6.86 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.40 (mt : the 5 aromatic H at position 6α); 7.47 (broad d, J = 8,5 Hz, 1H : 1' H_4); 7.52 (dd, J = 8.5 and 4 Hz, 1H : 1' H_5); 7.96 (broad d, J = 4 Hz, 1H : 1' H_6); 8.18 (s, 1H : CH=N); 8.38 (d, J = 10 Hz, 1H : CONH at position 1); 8.70 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.64 (s, 1H: OH).

Example 24

16.2 g of 2"-methylthiopyrimido[4,5-5γ,5δ]-pristinamycin I_E at 95% purity are introduced into a three-necked flask containing 130 cm^3 of methanol and then 551 cm^3 of 0.5 N sulphuric acid are added at 4°C followed by 19.94 g of Oxone® over 6 minutes. The mixture is stirred for 2 hours at 4°C and then for 18 hours at room temperature. The reaction mixture is cooled to 4°C, diluted with 150 cm^3 of dichloromethane and then the pH adjusted to 3 with a dilute sodium hydroxide solution. The aqueous phase is decanted off and then washed with twice 100 cm^3 of dichloromethane. The organic phases are combined, washed with 50 cm^3 of a saturated sodium chloride solution, dried and concentrated under reduced pressure (2.7 kPa) so as to obtain a final volume of 200 cm^3. To the chloromethylene solution obtained, placed in a three-necked flask, there are added 100 cm^3 of distilled water and, with vigorous stirring, 3 cm^3 of a 50% (w/v) solution of sodium bisulphite and then a saturated sodium

bicarbonate solution up to pH 6. After decantation, the aqueous phase is washed with twice 100 cm^3 of dichloromethane. The organic phases are combined, dried over sodium sulphate, filtered and concentrated to dryness at 40°C under reduced pressure (2.7 kPa) to give 15.3 g of a solid which is purified by flash chromatography [eluent: dichloromethane/methanol 95/5 by volume]. 10.2 g of product are thus obtained in the form of a yellow solid, which solid may be used as it is.

An analytical sample may be obtained by purification by flash chromatography [eluent: dichloromethane/methanol 98/2 by volume] of 0.6 g of product. After concentration of the fractions at 40°C under reduced pressure (2.7 kPa), trituration in 5 cm^3 of diethyl ether, filtration and drying at 50°C (90 Pa), 0.35 g of 2"-methylsulphonylpyrimido-[4,5-5γ,5δ]pristinamycin I_E is obtained in the form of a pale-yellow solid melting at 214°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.25 to 1.40 (mt, 2H : 1H of CH_2 at position 3β - 1H of CH_2 at position 3γ); 1.32 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.44 (dd, J = 17 and 5.5 Hz, 1H : 1H of CH_2 at position 5β); from 1.55 to 1.85 (mt : the 3H corresponding to CH_2 at position 2β and the other H of CH_2 at position 3γ); 2.08 (mt, 1H : the other H of CH_2 at position 3β); 2.86 (s, 6H : $ArN(CH_3)_2$); 2.95 (dd,

J = 12 and 4.5 Hz, 1H : 1H of CH_2 at position 4β); 3.11 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5β); 3.20 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); from 3.20 to 3.35 (mt, 1H : 1H of CH_2 at position 3δ); 3.27 (s, 6H : NCH_3 and $ArSO_2CH_3$); 3.51 (mt, 1H : the other H of CH_2 at position 3δ); 3.87 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.61 (dd, J = 7.5 and 6 Hz, 1H : CH at position 3α); 4.81(mt, 1H : CH at position 2α); 4.91 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.11 (dd, J = 12 and 4.5 Hz, 1H : CH at position 4α); 5.42 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.54 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.63 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.34 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.56 (d, J = 10 Hz, 1H : CONH at position 2); 6.87 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.40 (mt : the 5 aromatic H at position 6α); 7.49 (broad d, J = 8,5 Hz, 1H : 1' H_4); 7.54 (dd, J = 8.5 and 4 Hz, 1H : 1' H_5); 7.98 (broad d, J = 4 Hz, 1H : 1' H_6); 8.41 (d, J = 10 Hz, 1H : CONH at position 1); 8.53 (s, 1H : CH=N); 8.84 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.65 (s, 1H: OH).

Example 25

1.9 cm^3 of pyrrolidine are introduced into a three-necked flask containing 25 cm^3 of dioxane and 2 g of 2"-(4-methylbenzylsulphonyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E and then the mixture is heated at 90°C

for 3 hours. After concentrating the reaction mixture to dryness at 40°C under reduced pressure (2.7 kPa), the residue obtained is chromatographed on 150 g of silica [eluent: dichloromethane/methanol 96/4 by volume] to give 0.46 g of a cream-coloured solid which is recrystallized from 10 cm^3 of methanol. The crystals are filtered, rinsed with a minimum of methanol and then dried at 40°C under reduced pressure (90 Pa) to give 0.32 g of 2"-(1-pyrrolidinyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E in the form of white crystals melting at 255°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.40 (mt, 3H : 1H of CH_2 at position 3β - 1H of CH_2 at position 3γ and 1H of CH_2 at position 5β); 1.29 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.56 (mt, 1H : the other H of CH_2 at position 3γ); from 1.60 to 1.85 (mt: the 2H corresponding to CH_2 at position 2β); 1.93 (mt, 4H : the 2 CH_2 of pyrrolidine); 2.03 (mt, 1H : the other H of CH_2 at position 3β); 2.86 (s, 6H : $ArN(CH_3)_2$); 2.88 (d, J = 17.5 Hz, 1H : the other H of CH_2 at position 5β); 2.94 (dd, J = 12 and 4.5 Hz, 1H : 1H of CH_2 at position 4β); from 3.15 to 3.30 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.23 (s, 3H : NCH_3); from 3.45 to 3.60 (mt, 1H : the other H of CH_2 at position 3δ); 3.53 (mt, 4H : the 2 NCH_2 of pyrrolidine); 3.74 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.61 (dd, J = 8 and 7 Hz, 1H : CH at

position 3α); 4.78 (mt, 1H : CH at position 2α); 4.86 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.11 (dd, J = 12 and 4.5 Hz, 1H : CH at position 4α); 5.29 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.31 (mt, 1H : CH at position 5α); 5.62 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.87 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.38 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.55 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.86 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.40 (mt : the 5 aromatic H at position 6α); 7.43 (limiting AB, 2H : 1' H_4 and 1' H_5); 7.91 (mt, 1H : 1' H_6); 7.99 (s, 1H : CH=N); 8.39 (d, J = 10 Hz, 1H : CONH at position 1); 8.62 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.64 (s, 1H: OH).

2"-(4-Methylbenzylsulphonyl)pyrimido-[4,5-5γ,5δ]pristinamycin I_E may be prepared in the following manner:

1 litre of 1 N sulphuric acid is added to a three-necked flask containing 800 cm^3 of methanol and 24.6 g of 2"-(4-methylbenzylthio)pyrimido[4,5-5γ,5δ]-pristinamycin I_E. The mixture is cooled to 0°C and then 28.4 g of Oxone® are added. The stirring is maintained for 18 hours at room temperature and then the mixture is neutralized by slow addition of sodium bicarbonate so as to obtain a pH of 8 and then extracted with 3 times 1 litre of dichloromethane. The organic phases are combined, dried over magnesium sulphate, filtered

and concentrated to dryness at 45°C under reduced pressure (2.7 kPa) to give 30 g of a solid which is chromatographed on 1.2 kg of silica [eluent: dichloromethane/methanol/acetic acid, 89/10/1 by volume]. After concentration to dryness at 45°C under reduced pressure (2.7 kPa) of the fractions, the product is triturated in 100 cm^3 of diethyl ether, filtered and dried at 40°C under reduced pressure (90 Pa). 21.7 g of 2"-(4-methylbenzylsulphonyl)-pyrimido[4,5-5γ,5δ](4ζ-dimethylamino N oxide)-(4ζ-dedimethylamino)pristinamycin I_E are thus obtained in the form of a pale-yellow solid melting at 247°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.91 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); 0.99 (dd, J = 17 and 5.5 Hz, 1H : 1H of CH_2 at position 5β); 1.14 (mt, 1H : 1H of CH_2 at position 3β); 1.44 (mt, 1H : 1H of CH_2 at 3γ); 1.32 (d, J = 7 Hz, 3H : CH_3 at position 1γ); from 1.55 to 1.75 (mt, 3H : CH_2 at position 2β and the other H of CH_2 at position 3γ); 2.07 (mt, 1H : the other H of CH_2 at position 3β); 2.28 (s, 3H : $ArCH_3$); 3.10 (dd, J = 12 and 4 Hz, 1H : 1H of CH_2 at position 4β); 3.17 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5β); 3.24 (s, 3H : NCH_3); 3.27 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 3.47 and 3.58 (2 mts, 1H each: CH_2 at position 3δ); 3.58 and 3.73 (2 s, 3H each : $ArN(CH_3)_2$); 3.81 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.55 (mt, 1H : CH at position 3α); 4.58 and 4.79 (2 d, J = 14 Hz, 1H each : O_2SCH_2Ar);

4.84 (mt, 1H : CH at position 2α); 4.92 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.31 (dd, J = 12 and 4 Hz, 1H : CH at position 4α); 5.36 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.60 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.70 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.83 (d, J = 9 Hz, 1H : CONH at position 2); 7.08 (d, J = 8 Hz, 2H : aromatic H at the ortho position with respect to CH_3); 7.11 (d, J = 8 Hz, 2H : aromatic H at position 4δ); 7.19 (d, J = 8 Hz, 2H : aromatic H at the meta position with respect to CH_3); from 7.20 to 7.40 (mt : the 5 aromatic H at position 6α); 7.47 (broad d, J = 8.5 Hz, 1H : 1' H_4); 7.62 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 7.72 (dd, J = 8.5 and 4.5 Hz, 1H : 1' H_5); 7.85 (mt, 1H : 1' H_6); 8.41 (d, J = 10 Hz, 1H : CONH at position 1); 8.55 (s, 1H : CH=N); 8.75 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.65 (broad unresolved complex, 1H: OH).

4.8 g of 2"-(4-methylbenzylsulphonyl)-pyrimido[4,5-5γ,5δ](4ζ-dimethylamino N oxide)-(4ζ-dedimethylamino)pristinamycin I_E and 0.4 g of iron powder are introduced into a three-necked flask containing 50 cm^3 of glacial acetic acid. The mixture is heated for 2 minutes at 60°C, cooled, neutralized by addition of a 10% solution of sodium bicarbonate and then extracted with 100 cm^3 of dichloromethane. The organic phases are combined, dried over sodium

sulphate, filtered and concentrated to dryness at 40°C under reduced pressure (2.7 kPa) to give 4.35 g of a chestnut-coloured solid which is recrystallized from 50 cm^3 of hot isopropanol. After filtration, washing of the crystals with 10 cm^3 of diisopropyl ether and drying at 40°C under reduced pressure (90 kPa), 2.06 g of 2"-(4-methylbenzylsulphonyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E are obtained in the form of a beige solid melting at 188°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.91 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.45 (dd, J = 17 and 5.5 Hz, 1H : 1H of CH_2 at position 5β); from 1.55 to 1.75 (mt: the 2H corresponding to 1H of CH_2 at position 2β and the other H of CH_2 at position 3γ); 1.74 (mt, 1H : the other H of CH_2 at position 2β); 2.08 (mt, 1H : the other H of CH_2 at position 3β); 2.30 (s, 3H : $ArCH_3$); 2.81 (s, 6H : $ArN(CH_3)_2$); 2.95 (dd, J = 12 and 4.5 Hz, 1H : 1H of CH_2 at position 4β); 3.01 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5β); 3.19 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); from 3.20 to 3.35 (mt, 1H : 1H of CH_2 at position 3δ); 3.26 (s, 3H : NCH_3); 3.51 (mt, 1H : the other H of CH_2 at position 3δ); 3.88 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.50 and 4.74 (2 d, J = 14 Hz, 1H each : O_2SCH_2Ar); 4.61 (dd, J = 7.5 and 6 Hz, 1H : CH at position 3α); 4.80 (mt, 1H

: CH at position 2α); 4.90 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.08 (dd, J = 12 and 4.5 Hz, 1H : CH at position 4α); 5.40 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.54 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.66 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.89 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.29 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.53 (d, J = 10 Hz, 1H : CONH at position 2); 6.84 (d, J = 8 Hz, 2H : aromatic H at position 4δ); 7.12 (d, J = 8 Hz, 2H : aromatic H at the ortho position with respect to CH_3); from 7.10 to 7.35 (mt : the 5 aromatic H at position 6α); 7.20 (d, J = 8 Hz, 2H : aromatic H at the meta position with respect to CH_3); 7.48 (broad d, J = 8.5 Hz, 1H : 1' H_4); 7.53 (dd, J = 8.5 and 4 Hz, 1H : 1' H_5); 7.96 (broad d, J = 4 Hz, 1H : 1' H_6); 8.39 (d, J = 10 Hz, 1H : CONH at position 1); 8.50 (s, 1H : CH=N); 8.80 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.64 (s, 1H: OH).

2"-(4-Methylbenzylthio)pyrimido[4,5-5γ,5δ]-pristinamycin I_E may be prepared in the following manner:

4.3 g of 5δ-dimethylaminomethylene-pristinamycin I_A, 1 g of (4-methylbenzyl)isothiourea hydrochloride are introduced into a three-necked flask containing 35 cm^3 of dimethylformamide and then 1.8 cm^3 of N,N-diisopropylamine are added dropwise. The mixture is heated for 3 hours at 60°C, cooled and then diluted with 200 cm^3 of distilled water. The precipitate formed

is filtered to give 1 g of product which is purified by HPLC on 450 g of 10 µm C_8 silica [eluent: water-acetonitrile 50/50 by volume containing 0.1% trifluoroacetic acid]. The fractions are combined, the acetonitrile removed at 40°C under reduced pressure (2.7 kPa) and the aqueous phase adjusted to pH 7-8 with water saturated with sodium bicarbonate. The mixture is extracted with 3 times 80 cm^3 of dichloromethane, the organic phases are combined, dried over magnesium sulphate, filtered, concentrated to dryness and then dried at 40°C under reduced pressure (90 Pa) to give 1.09 g of 2"-(4-methylbenzylthio)pyrimido-[4,5-5γ,5δ]pristinamycin I_E in the form of a cream-coloured solid melting at 222°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.91 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.35 (mt, 3H : 1H of CH_2 at position 3β - 1H of CH_2 at position 3γ and 1H of CH_2 at position 5β); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); from 1.55 to 1.80 (mt: the 2H corresponding to CH_2 at position 2β); 1.59 (mt, 1H: the other H of CH_2 at position 3γ); 2.05 (mt, 1H: the other H of CH_2 at position 3β); 2.32 (s, 3H : $ArCH_3$); 2.86 (s, 6H : $ArN(CH_3)_2$); 2.91 (dd, J = 12 and 4 Hz, 1H : 1H of CH_2 at position 4β); 2.94 (d, J = 17.5 Hz, 1H : the other H of CH_2 at position 5β); from 3.15 to 3.30 (mt, 1H : 1H of CH_2 at position 3δ); 3.21 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 3.25 (s, 3H, NCH_3); 3.50 (mt, 1H : the other H of

CH_2 at position 3δ); 3.76 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.27 and 4.39 (2 d, J = 13.5 Hz, 1H each : $ArSCH_2Ar$); 4.61 (dd, J = 7.5 and 5.5 Hz, 1H : CH at position 3α); 4.79 (mt, 1H : CH at position 2α); 4.88 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.07 (dd, J = 12 and 4 Hz, 1H : CH at position 4α); 5.32 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.39 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.64 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.87 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.33 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.53 (d, J = 10 Hz, 1H : CONH at position 2); 6.84 (d, J = 8 Hz, 2H : aromatic H at position 4δ); 7.11 (d, J = 8 Hz, 2H : aromatic H at the ortho position with respect to CH_3); from 7.15 to 7.40 (mt : the 5 aromatic H at position 6α); 7.32 (d, J = 8 Hz, 2H : aromatic H at the meta position with respect to the CH_3); 7.44 (broad d, J = 8.5 Hz, 1H : 1' H_4); 7.48 (dd, J = 8.5 and 4 Hz, 1H : 1' H_5); 7.93 (broad d, J = 4 Hz, 1H : 1' H_6); 8.19 (s, 1H : CH=N); 8.38 (d, J = 10 Hz, 1H : CONH at position 1); 8.70 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.63 (s, 1H: OH).

Example 26

By carrying out the procedure as in Example 25 but starting with 40 cm^3 of dioxane, 2 g of 2"-(4-methylbenzylsulphonyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E, 1.02 cm^3 of azetidine and after heating for 45 minutes at 60°C, a precipitate is

obtained after cooling which is filtered, washed with 10 cm^3 of diisopropyl ether and then recrystallized from 15 cm^3 of methanol to give after filtration, drying at 40°C under reduced pressure (90 Pa), 1.05 g of 2"-(1-azetidinyl)pyrimido[4,5-5γ,5δ]pristinamycin I_E in the form of a white powder melting at 243°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.35 (mt, 3H : 1H of CH_2 at position 3β - 1H of CH_2 at position 3γ and 1H of CH_2 at position 5β); 1.29 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.56 (mt, 1H : the other H of CH_2 at position 3γ); 1.65 and 1.72 (2 mts, 1H each : CH_2 at position 2β); 2.05 (mt, 1H : the other H of CH_2 at position 3β); 2.33 (mt, 2H : CH_2 of azetidine); 2.86 (d, J = 17.5 Hz, 1H : the other H of CH_2 at position 5β); 2.88 (s, 6H : $ArN(CH_3)_2$); 2.92 (dd, J = 12 and 4.5 Hz, 1H : 1H of CH_2 at position 4β); from 3.10 to 3.35 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.22 (s, 3H : NCH_3); 3.48 (mt, 1H : the other H of CH_2 at position 3δ); 3.72 Hz(d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.09 (mt, 4H : the 2 NCH_2 of azetidine); 4.59 (dd, J = 8 and 6 Hz, 1H : CH at position 3α); 4.78 (mt, 1H : CH at position 2α); 4.88 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.12 (dd, J = 12 and 4.5 Hz, 1H : CH at position 4α); 5.29 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.31 (broad d, J = 6 Hz, 1H : CH at position 5α); 5.62 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.87

(broad q, J = 7 Hz, 1H : CH at position 1β); 6.40 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.55 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.87 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.15 to 7.35 (mt : the 5 aromatic H at position 6α); 7.42 (limiting AB, 2H : 1' H_4 and 1' H_5); 7.90 (mt, 1H : 1' H_6); 7.97 (s, 1H : CH=N); 8.40 (d, J = 10 Hz, 1H : CONH at position 1); 8.63 (d, J = 8.5 Hz, 1H : CONH at position 6).

Example 27

By carrying out the procedure as in Example 22 but starting with 5 cm^3 of dimethylformamide, 1.84 g of 5δ-dimethylaminomethylenepristinamycin I_A, 0.41 g of 4-amidinopyridinium hydrochloride, 0.235 g of sodium bicarbonate and heating for 4 hours at 65°C, a solution is obtained after cooling which is diluted with 40 cm^3 of ethyl acetate and 50 cm^3 of distilled water. After decantation, the aqueous phase is washed with twice 40 cm^3 of ethyl acetate, the organic phases are pooled and then washed with 200 cm^3 of brine, dried over magnesium sulphate, filtered and concentrated at 40°C under reduced pressure (2.7 kPa) to give a residue which is chromatographed on 90 g of silica [eluent: dichloromethane/methanol 96/4 by volume]. 0.535 g of a product is obtained which is purified with 1.37 g of an identical product obtained by a similar preparation by HPLC on 450 g of 10 µm C_8 silica [eluent: water-acetonitrile 35/65 by volume containing 0.1%

trifluoroacetic acid]. The fractions are combined, the acetonitrile removed at 40°C under reduced pressure (2.7 kPa) and the aqueous phase adjusted to pH 7-8 with water saturated with sodium bicarbonate. The mixture is extracted with 3 times 100 cm^3 of dichloromethane, the organic phases are combined, dried over magnesium sulphate, filtered, concentrated to dryness and then dried at 40°C under reduced pressure 90 Pa) to give 0.73 g of a white solid which is triturated in 10 cm^3 of diisopropyl ether, filtered and dried at 40°C (90 Pa). 0.67 g of 2"-(4-pyridyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E is thus obtained in the form of a white solid melting at 277°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.41 (dd, J = 17 and 6 Hz, 1H : 1H of CH_2 at position 5β); 1.60 (mt, 1H : the other H of CH_2 at position 3γ); from 1.60 to 1.85 (mt : the 2H corresponding to CH_2 at position 2β); 2.07 (mt, 1H : the other H of CH_2 at position 3β); 2.63 (s, 6H : $ArN(CH_3)_2$); 2.92 (dd, J = 12 and 4 Hz, 1H : 1H of CH_2 at position 4β); 3.10 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5β); from 3.20 to 3.35 (mt, 2H : 1H of CH_2 at position 3δ and the other H of CH_2 at position 4β); 3.27 (s, 3H : NCH_3); 3.51 (mt, 1H : the other H of CH_2 at position 3δ); 3.88 (d, J = 17 Hz, 1H : 1H of CH_2

at position 5ε); 4.61 (dd, J = 7.5 and 6 Hz, 1H : CH at position 3α); 4.80 (mt, 1H : CH at position 2α); 4.88 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.06 (dd, J = 12 and 4 Hz, 1H : CH at position 4α); 5.41 (broad d, J = 6 Hz, 1H : CH at position 5α); 5.52 (d, J = 17 Hz : the other H of CH_2 at position 5ε); 5.64 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.38 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.54 (d, J = 10 Hz, 1H : CONH at position 2); 6.86 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.40 (mt : the 5 aromatic H at position 6α); 7.49 (broad d, J = 8.5 Hz, 1H : 1'H_4); 7.57 (dd, J = 8.5 and 4 Hz, 1H : 1' H_5); 8.04 (broad d, J = 4 Hz, 1H : 1' H_6); 8.27 (d, J = 5 Hz, 2H : aromatic H at position β of pyridine); 8.38 (d, J = 10 Hz, 1H : CONH at position 1); 8.48 (s, 1H : CH=N; 8.72 (d, J = 8.5 Hz, 1H : CONH at position 6); 8.75 (d, J = 5 Hz, 2H : aromatic H at position α of pyridine; 11.66 (s, 1H : OH).

Example 28

6 g of 5δ-dimethylaminomethylenepristinamycin I_A, 1.33 g of 2-amidinopyridinium hydrochloride are introduced into a three-necked flask containing 35 cm^3 of dimethylformamide and then 3.4 cm^3 of N,N-diiso-propylamine are added dropwise. The mixture is heated for 4 hours at 65°C, cooled and then diluted with 500 cm^3 of distilled water saturated with sodium chloride. The precipitate formed is filtered and then

taken up in 300 cm^3 of dichloromethane. The solution obtained is dried over sodium sulphate, filtered and concentrated to dryness under reduced pressure at 40°C (2.7 kPa) to give 4.36 g of a product which is purified by chromatography on 220 g of silica [eluent: dichloromethane/methanol 95/5 by volume]. After concentrating the fractions to dryness under reduced pressure at 40°C (2.7 kPa), 3.15 g of a solid are obtained, which solid is recrystallized from 20 cm^3 of isopropanol. The crystals are filtered, washed with 20 cm^3 of diisopropyl ether and then dried at 40°C (90 Pa) to give 1.08 g of 2"-(2-pyridyl)pyrimido[4,5-5γ,5δ]pristinamycin IE in the form of a white powder melting at 214°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.35 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.51 (dd, J = 17 and 6 Hz, 1H : 1H of CH_2 at position 5β); from 1.55 to 1.80 (mt : the 2H corresponding to CH_2 at position 2β); 1.59 (mt, 1H : the other H of CH_2 at position 3γ); 2.06 (mt, 1H : the other H of CH_2 at position 3β); 2.64 (s, 6H : $ArN(CH_3)_2$); 2.93 (dd, J = 12 and 4.5 Hz, 1H : 1H of CH_2 at position 4β); 3.13 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5β); from 3.15 to 3.30 (mt, 1H : 1H of CH_2 at position 3δ); 3.22 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 3.26 (s, 3H : NCH_3); 3.51 (mt, 1H : the

other H of CH_2 at position 3δ); 3.89 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.60 (dd, J = 8 and 6 Hz, 1H : CH at position 3α); 4.80 (mt, 1H : CH at position 2α); 4.90 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.12 (dd, J = 12 and 4.5 Hz, 1H : CH at position 4α); 5.42 (broad d, J = 6 Hz, 1H : CH at position 5α); 5.52 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.65 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.87 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.28 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.56 (d, J = 10 Hz, 1H : CONH at position 2); 6.85 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.15 to 7.40 (mt : the 5 aromatic H at position 6α); 7.35 (mt, 1H : H at position 5 of pyridine); 7.46 (broad d, J = 8.5 Hz, 1H : 1' H_4); 7.51 (dd, J = 8.5 and 4 Hz, 1H : 1' H_5); 7.82 (split t, J = 8 and 1.5 Hz, 1H : H at position 4 of pyridine); 7.99 (broad d, J = 4 Hz, 1H : 1' H_6); 8.41 (d, J = 10 Hz, 1H : CONH at position 1); 8.47 (d, J = 8 Hz, H at position 3 of pyridine); 8.56 (s, 1H : CH=N); 8.72 (d, J = 8.5 Hz, 1H : CONH at position 6); 8.82 (broad d, J = 5 Hz, 1H : H at position 6 of pyridine); 11.65 (s, 1H : OH).

Example 29

By carrying out the procedure as in Example 22 but starting with 4 cm^3 of dimethylformamide, 0.92 g of 5δ-dimethylaminomethylenepristinamycin I_A, 0.22 g of benzamidine hydrochloride and 0.12 g of sodium bicarbonate and after 4 hours at 60°C, 1 g of a residue

which is chromatographed on 170 g of silica [eluent: dichloromethane/methanol 96/4 by volume] is obtained after cooling, addition of 50 cm^3 of distilled water and 20 cm^3 of ethyl acetate to the reaction mixture, washing of the aqueous phase with twice 20 cm^3 of ethyl acetate, decantation of the organic phase which is dried over magnesium sulphate, filtered and concentrated to dryness at 40°C under reduced pressure (2.7 kPa). After concentration to dryness at 40°C under reduced pressure (2.7 kPa) of the fractions, the product is triturated in 10 cm^3 of diisopropyl ether, filtered and dried at 40°C under reduced pressure (90 Pa) to give 0.49 g of 2"-phenylpyrimido[4,5-5γ,5δ]pristinamycin I_E in the form of a white powder melting at 201°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.35 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.40 (dd, J = 17 and 6 Hz, 1H : 1H of CH_2 at position 5β); 1.59 (mt : 1H : the other H of CH_2 at position 3γ); 1.65 (mt: 1H corresponding to 1H of CH_2 at position 2β); 1.74 (mt, 1H : the other H of CH_2 at position 2β); 2.06 (mt, 1H : the other H of CH_2 at position 3β); 2.64 (s, 6H : $ArN(CH_3)_2$); 2.93 (dd, J = 12 and 4 Hz, 1H : 1H of CH_2 at position 4β); 3.09 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5β); from 3.15 to 3.30 (mt, 2H : 1H of CH_2 at position 3δ and the other H of CH_2 at position 4β); 3.27 (s, 3H : NCH_3);

3.50 (mt, 1H : the other H of CH_2 at position 3δ); 3.87 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.61 (dd, J = 8 and 6 Hz, 1H : CH at position 3α); 4.81 (mt, 1H, CH at position 2α); 4.90 (dd, J = 10 and 1.5 Hz, 1H : CH at position 1α); 5.10 (dd, J = 12 and 4 Hz, 1H : CH at position 4α); 5.41 (broad d, J = 6 Hz, 1H : CH at position 5α); 5.49 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.65 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.90 (split q, J = 7 and 1.5 Hz, 1H : CH at position 1β); 6.30 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.56 (d, J = 10 Hz, 1H : CONH at position 2); 6.87 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.40 (mt : the 5 aromatic H at position 6α); from 7.40 to 7.50 (mt, 3H : aromatic H at the para and meta positions of the phenyl); 7.48 (dd, J = 8.5 and 1.5 Hz, 1H : 1' H_4); 7.56 (dd, J = 8.5 and 4 Hz, 1H : 1' H_5); 8.03 (dd, J = 4 and 1.5 Hz, 1H : 1' H_6); from 8.35 to 8.45 (mt, 3H : aromatic H at the ortho position of the phenyl and CONH at position 1); 8.44 (s, 1H : CH=N); 8.70 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.66 (s, 1H : OH).

Example 30

By carrying out the procedure as in Example 22 but starting with 10 cm^3 of dimethylformamide, 2 g of 5δ-dimethylaminomethylenepristinamycin I_A, 0.59 g of 3-aminobenzamidine hydrochloride and 0.47 g of sodium bicarbonate and after 4 hours at 60°C, a residue which is chromatographed on 200 g of silica [eluent:

dichloromethane/methanol 96/4 by volume] to give 1.06 g of a solid is obtained after cooling, addition of 50 cm^3 of distilled water and 40 cm^3 of ethyl acetate to the reaction mixture, washing of the aqueous phase with twice 40 cm^3 of ethyl acetate, decantation of the organic phase which is dried over magnesium sulphate, filtered and concentrated to dryness at 40°C under reduced pressure (2.7 kPa). The solid is purified by HPLC on 450 g of 10 µm C_8 silica [eluent: water-acetonitrile 65/35 by volume containing 0.1% trifluoroacetic acid], the fractions are combined, the acetonitrile removed at 40°C under reduced pressure (2.7 kPa) and the aqueous phase adjusted to pH 7-8 with water saturated with sodium bicarbonate. The precipitate formed is filtered, washed with diisopropyl ether, dried at 40°C under reduced pressure (90 Pa) to give 0.31 g of 2"-(3-aminophenyl)pyrimido[4,5-5γ,5δ]pristinamycin I_E in the form of a pale-yellow solid melting at 212°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.93 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.43 (dd, J = 17 and 6 Hz, 1H : 1H of CH_2 at position 5β); from 1.50 to 1.75 (mt : the 2H corresponding to the other H of CH_2 at position 3γ and to 1H of CH_2 at position 2β); 1.76 (mt, 1H : the other H of CH_2 at position 2β); 2.08 (mt, 1H : the other H of

CH_2 at position 3β); 2.69 (s, 6H : $ArN(CH_3)_2$); 2.94 (dd, J = 12.5 and 4.5 Hz, 1H : 1H of CH_2 at position 4β); 3.10 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5β); from 3.15 to 3.35 (mt, 2H : 1H of CH_2 at position 3δ and the other H of CH_2 at position 4β); 3.28 (s, 3H : NCH_3); 3.51 (mt, 1H : the other H of CH_2 at position 3δ); 3.76 (broad s, 2H : $ArNH_2$); 3.88 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.63 (dd, J = 8 and 6 Hz, 1H : CH at position 3α); 4.82 (mt, 1H : CH at position 2α); 4.90 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.11 (dd, J = 12.5 and 4.5 Hz, 1H : CH at position 4α); 5.41 (broad d, J = 6 Hz, 1H : CH at position 5α); 5.49 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.66 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.90 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.31 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.55 (d, J = 10 Hz, 1H : CONH at position 2); 6.80 (dd, J = 8 and 1.5 Hz, 1H : aromatic H at position 4 of 3-aminophenyl); 6.85 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.40 (mt : the 6H corresponding to the 5 aromatic H at position 6α and to the aromatic H at position 5 of 3-aminophenyl); 7.49 (broad d, J = 8.5 Hz, 1H : 1' H_4); 7.55 (dd, J = 8.5 and 4 Hz, 1H : 1' H_5); 7.75 (broad s, 1H : aromatic H at position 2 of 3-aminophenyl); 7.82 (broad d, 1H : aromatic H at position 6 of 3-aminophenyl); 8.03 (dd, J = 4 and 1.5 Hz, 1H : 1' H_6); 8.40 (d, J = 10 Hz, 1H : CONH at position 1); 8.42 (s, 1H : CH=N); 8.70 (d, J =

8.5 Hz, 1H : CONH at position 6); 11.66 (s, 1H : OH).

Example 31

By carrying out the procedure as in Example 22 but starting with 45 cm^3 of dimethylformamide, 5 g of 5δ-dimethylaminomethylenepristinamycin I_B, 0.64 g of S-methylisothiouronium sulphate and 0.77 g of sodium bicarbonate and after 18 hours at 60°C, 3.16 g of a residue which is chromatographed on 250 g of silica [eluent: dichloromethane/methanol 95/5 by volume] to give 1.2 g of a solid are obtained after cooling, addition of 200 cm^3 of distilled water and 150 cm^3 of ethyl acetate to the reaction mixture, washing of the aqueous phase with twice 150 cm^3 of ethyl acetate, decantation of the organic phase which is washed with 250 cm^3 of distilled water, dried over magnesium sulphate, filtered and concentrated to dryness at 40°C under reduced pressure (2.7 kPa). The solid is purified by HPLC on 450 g of 10 µm C_8 silica [eluent: water-acetonitrile 65/35 by volume containing 0.1% trifluoroacetic acid], the fractions are combined, the acetonitrile removed at 40°C under reduced pressure (2.7 kPa), the aqueous phase adjusted to pH 7-8 with water saturated with sodium bicarbonate and extracted with twice 100 cm^3 of dichloromethane. The organic phase is decanted off, dried over magnesium sulphate, filtered and then concentrated to dryness and then dried at 40°C under reduced pressure (90 Pa) to give 0.45 g of 2"-methylthiopyrimido[4,5-5γ,5δ](4ζ-

methylamino)(4ζ-dedimethylamino)pristinamycin I_E in the form of a pale-yellow solid melting at 282°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.91 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.40 (mt, 3H : 1H of CH_2 at position 3β - 1H of CH_2 at position 3γ and 1H of CH_2 at position 5β); 1.32 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.58 (mt, 1H : the other H of CH_2 at position 3γ); from 1.60 to 1.85 (mt : the 2H corresponding to CH_2 at position 2β); Hz2.06 (mt, 1H : the other H of CH_2 at position 3β); 2.64 (s, 3H : $ArSCH_3$); 2.77 (s, 3H : $ArNCH_3$); 2.89 (dd, J = 12 and 4.5 Hz, 1H : 1H of CH_2 at position 4β); 2.97 (d, J = 17.5 Hz, 1H : the other H of CH_2 at position 5β); 3.20 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); from 3.20 to 3.35 (mt, 1H : 1H of CH_2 at position 3δ); 3.25 (s, 3H : NCH_3); 3.50 (mt, 1H : the other H of CH_2 at position 3δ); from 3.65 to 3.85 (broad unresolved complex, 1H : ArNH); 3.75 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.61 (dd, J = 8 and 5.5 Hz, 1H : CH at position 3α); 4.80 (mt, 1H : CH at position 2α); 4.88 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.03 (dd, J = 12 and 4.5 Hz, 1H : CH at position 4α); 5.32 (broad d, J = 6 Hz, 1H : CH at position 5α); 5.39 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.65 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.18 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.51 (d, J = 10 Hz, 1H : CONH at position 2); 6.78 (d, J = 8 Hz, 2H : aromatic H

at position 4δ); from 7.20 to 7.40 (mt : the 5 aromatic H at position 6α); 7.46 (broad d, J = 8.5 Hz, 1H : 1' H_4); 7.50 (dd, J = 8.5 and 4 Hz, 1H : 1' H_5); 7.94 (broad d, J = 4 Hz, 1H : 1' H_6); 8.17 (s, 1H : CH=N); 8.38 (d, J = 10 Hz, 1H : CONH at position 1); 8.67 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.62 (s, 1H : OH).

Example 32

97 mg of 2"-(1-pyrrolidinylpyrimido[4,5-5γ,5δ]pristinamycin I_E, 5.4 mg of ethylene glycol, 65 mg of acetic acid and 20 mg of tetra-n-butylammonium periodate are introduced into a round-bottomed flask containing 0.4 cm^3 of dichloromethane. The mixture is stirred for 4 hours at room temperature and then the reaction mixture is taken up in 8 cm^3 of water and 4 cm^3 of dichloromethane. The organic phase is decanted off, washed with 4 times 8 cm^3 of distilled water, decanted off, dried and then concentrated to dryness at 40°C under reduced pressure (2.7 kPa) to give 70 mg of a solid which is purified by flash chromatography with 210 mg of an identical product obtained from a similar preparation on 15 g of silica [eluent: dichloromethane/methanol 97/3 by volume] to give after concentration to dryness of the fractions, trituration in 4 cm^3 of diethyl ether, filtration and drying at 20°C under reduced pressure (90 Pa), 98 mg of 2"-(1-pyrrolidinyl)pyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E in the form of a

cream-coloured powder melting at 222°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.48 (dd, J = 17 and 6 Hz, 1H : 1H of CH_2 at position 5β); from 1.50 to 1.85 (mt : the 3H corresponding to the other H of CH_2 at position 3γ and to CH_2 at position 2β); 1.95 (mt, 4H : the 2 CH_2 of pyrrolidine); 2.04 (mt, 1H : the other H of CH_2 at position 3β); Hz2.62 (s, 3H : $ArNCH_3$); 2.91 (dd, J = 12.5 and 4.5 Hz, 1H : 1H of CH_2 at position 4β); 2.92 (d, J = 17.5 Hz, 1H : the other H of CH_2 at position 5β); from 3.15 to 3.35 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.22 (s, 3H : NCH_3); from 3.45 to 3.65 (mt, 5H : the other H of CH_2 at position 3δ and the 2 NCH_2 of pyrrolidine); 3.73 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.60 (dd, J = 6.5 and 5.5 Hz, 1H : CH at position 3α); 4.78 (mt, 1H : CH at position 2α); 4.88 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.14 (dd, J = 12 and 4.5 Hz, 1H : CH at position 4α); 5.29 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.31 (unresolved complex, 1H : CH at position 5α); 5.64 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.87 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.28 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.56 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.82 (d, J = 8 Hz, 2H : aromatic H at

position 4δ); from 7.20 to 7.40 (mt : the 5 aromatic H at position 6α); 7.42 (limiting AB, 2H : 1' H_4 and 1' H_5); 7.90 (mt, 1H : 1' H_6); 7.98 (s, 1H : CH=N); 8.42 (d, J = 10 Hz, 1H : CONH at position 1); 8.62 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.65 (s, 1H : OH).

Example 33

30 g of pristinamycin I_A, 2.42 g of 3-aminoacrolein and then 25.8 g of ammonium acetate are introduced into a three-necked flask containing 400 cm^3 of methanol. The mixture is refluxed for 3 days and then diluted with 1 litre of distilled water. The precipitate obtained is filtered, dried and then chromatographed on 1 kg of silica (eluent: dichloromethane/methanol 98/2 by volume). The solid obtained is purified by HPLC on 10 µm C_8 silica (eluent: water-acetonitrile 70/30 containing 0.1% trifluoroacetic acid. The fractions are combined, the acetonitrile removed at 40°C under reduced pressure (2.7 kPa) and the aqueous phase adjusted to pH 8 with 3 cm^3 of water saturated with sodium bicarbonate. The precipitate obtained is filtered, rinsed with 10 cm^3 of distilled water and then 10 cm^3 of diethyl ether to give after drying at 40°C under reduced pressure (90 Pa), 0.45 g of pyrido[2,3-5γ,5δ]pristinamycin I_E in the form of a white solid melting at around 170-180°C (dec.).

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2

at position 3γ); 1.34 (d, J = 7 Hz, 3H : CH_3 at position 1γ); from 1.55 to 1.85 (mt, 4H : the other H of CH_2 at position 3γ - CH_2 at position 2β and 1H of CH_2 at position 5β); 2.04 (mt, 1H : the other H of CH_2 at position 3β); 2.91 (s, 6H : $ArN(CH_3)_2$); 2.95 (dd, J = 12 and 5 Hz, 1H : 1H of CH_2 at position 4β); 3.17 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 3.24 (s, 3H : NCH_3); 3.30 (mt, 1H : 1H of CH_2 at position 3δ); 3.43 (broad d, J = 17 Hz, 1H : the other H of CH_2 at position 5β); 3.52 (mt, 1H : the other H of CH_2 at position 3δ); 3.91 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.58 (dd, J = 7 and 5.5 Hz, 1H : CH at position 3α); 4.81 (mt, 1H : CH at position 2α); 4.87 (dd, J = 10 and 1.5 Hz, 1H : CH at position 1α); 5.13 (dd, J = 12 and 5 Hz, 1H : CH at position 4α); 5.43 (mt, 1H : CH at position 5α); 5.46 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.65 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.87 (dq, J = 7 and 1.5 Hz, 1H : CH at position 1β); 6.40 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.58 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.85 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.40 (mt : the 5 aromatic H at position 6α); from 7.30 to 7.45 (mt, 1H : aromatic H at position β of N); 7.43 (d, J = 8 Hz, 1H : 1' H_4); 7.56 (dd, J = 8 and 4 Hz, 1H : 1' H_5); 7.61 (mt, 1H : aromatic H at position γ of N); 8.13 (mt, 1H : 1' H_6); 8.38 (d, J = 4 Hz, 1H : aromatic H at position α of N); 8.42 (d, J = 10 Hz, 1H : CONH at position 1); 8.69 (d,

J = 8.5 Hz, 1H : CONH at position 6); 11.59 (s, 1H : OH).

3-Aminoacrolein may be prepared according to R.P. Thummel & D.K. Kohli, J. Org. Chem., 42, 2742-2747 (1977).

Example 34

By carrying out the procedure as in Example 6 but starting with 11.4 g of 5δ-methylenepristinamycin I_A in 200 cm^3 of acetone, 3.8 g of 1-(2-oxopentyl)-pyridinium bromide, 10 g of ammonium acetate and heating for 3 hours under reflux, a solid is obtained which is chromatographed on 100 g of silica (eluent: acetonitrile) and then by HPLC on 450 g of 10 µm C_8 silica (eluent: water-acetonitrile 70/30 by volume, containing 0.1% trifluoroacetic acid). The fractions are combined, the acetonitrile removed at 40°C under reduced pressure (2.7 kPa) and the pH of the aqueous phase adjusted to 8 by addition of water saturated with sodium bicarbonate. The precipitate is filtered, washed with 20 cm^3 of distilled water and dried at 40°C under reduced pressure (90 Pa) to give 0.8 g of 2"-propylpyrido[2,3-5γ,5δ]pristinamycin I_E in the form of a white solid melting at 172°C.

^1H NMR spectrum (400 MHz, $CDCl_3$): 0.93 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); 0.98 (t, J = 7.5 Hz, 3H : CH_3 of propyl); from 1.20 to 1.35 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.30 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.58 (mt,

1H : the other H of CH_2 at position 3γ); from 1.50 to 1.90 (mt : the 3H corresponding to CH_2 at position 2β and to 1H of CH_2 at position 5β); 1.70 (mt, 2H : central CH_2 of propyl); 2.03 (mt, 1H : the other H of CH_2 at position 3β); 2.68 (t, J = 8 Hz, 2H : $ArCH_2$ of propyl); 2.84 (s, 6H : $ArN(CH_3)_2$); 2.97 (dd, J = 13 and 5.5 Hz, 1H : 1H of CH_2 at position 4β); from 3.15 to 3.35 (mt, 3H : the other H of CH_2 at position 5β - the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.21 (s, 3H : NCH_3); 3.49 (mt, 1H : the other H of CH_2 at position 3δ); 3.92 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.60 (dd, J = 8 and 5.5 Hz, 1H : CH at position 3α); 4.79 (mt, 1H : CH at position 2α); 4.87 (dd, J = 10 and 1 Hz, 1H : CH at position 1α); 5.28 (dd, J = 10 and 5.5 Hz, 1H : CH at position 4α); from 5.35 to 5.50 (mt, 2H : CH at position 5α and the other H of CH_2 at position 5ε); 5.63 (d, J = 8 Hz, 1H : CH at position 6α); 5.88 (split q, J = 7 and 1 Hz, 1H : CH at position 1β); 6.36 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.58 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.84 (d, J = 8 Hz, 2H : aromatic H at position 4δ); 6.94 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); from 7.20 to 7.45 (mt : the 8H corresponding to the 5 aromatic H at position 6α - to the aromatic H at position γ with respect to N - to 1' H_5 and to 1' H_4); 7.86 (dd, J = 4 and 1 Hz, 1H : 1' H_6); 8.43 (d, J = 10 Hz, 1H : CONH at position 1); 8.66 (d, J = 8 Hz, 1H : CONH at position 6); 11.64 (s,

1H : OH).

1-(2-Oxopentyl)pyridinium bromide may be prepared by analogy with 1-(2-oxopentyl)pyridinium iodide as described by R.P. SONI, J.P. SAXENA, J. Indian Chem. Soc., 58, 885-887 (1981).

3.8 g of 1-bromo-2-pentanone and 9.2 cm^3 of pyridine are introduced into a three-necked flask containing 25 cm^3 of ethanol and then the mixture is heated for 3 hours under reflux. After concentrating to dryness at 40°C under reduced pressure (2.7 kPa), the residue is taken up in 200 cm^3 of diisopropyl ether. After filtration, washing with 50 cm^3 of diethyl ether, the precipitate is dried to give 3.8 g of a pale-yellow solid of 80% purity melting at 72°C and which is used as it is.

1-bromo-2-pentanone may be prepared according to H.J. HA, Synth. Commun., 24, 2557, (1994).

Example 35

By carrying out the procedure as in Example 6 but starting with 30 g of 5δ-methylenepristinamycin I_A in 200 cm^3 of acetone, 10 g of 1-(3-methyl-2-oxobutyl)-pyridinium bromide, 26.3 g of ammonium acetate and heating for 3 hours under reflux, 34 g of a solid are obtained, which solid is purified by 2 successive chromatographies on 1 kg of silica (eluent: methylene chloride-acetonitrile-water: 96/2/2 by volume) and then 700 g of silica (eluent: methylene chloride and then methylene chloride-methanol-acetonitrile gradient:

99/0.5/0.5 to 98/1/1 by volume). After 2 recrystallizations from the methanol, 4.3 g of product are obtained of which 2 g are purified by HPLC on 450 g of 10 µm C_8 silica (eluent: water-acetonitrile 70/30 by volume, containing 0.1% trifluoroacetic acid). The fractions are combined, the acetonitrile removed at 40°C under reduced pressure (2.7 kPa) and the pH of the aqueous phase adjusted to 8 by addition of water saturated with sodium bicarbonate. The precipitate is filtered, washed with 20 cm^3 of water and then with 20 cm^3 of diisopropyl ether. After recrystallization from 15 cm^3 of methanol, filtration, washing with 10 cm^3 of methanol and 10 cm^3 of diisopropyl ether and then drying at 40°C under reduced pressure (90 Pa), 0.75 g of 2"-isopropylpyrido[2,3-5γ,5δ]pristinamycin I_E is obtained in the form of white needles melting at 263°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$): 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.35 (mt, 11H : 1H of CH_2 at position 3β - 1H of CH_2 at position 3γ - CH_3 at position 1γ and the 2 CH_3 of isopropyl); 1.58 (mt, 1H : the other H of CH_2 at position 3γ); 1.66 and 1.75 (2 mts, 1H each : CH_2 at position 2β); 1.89 (mt : 1H corresponding to 1H of CH_2 at position 5β); 2.03 (mt, 1H : the other H of CH_2 at position 3β); 2.85 (s, 6H : $ArN(CH_3)_2$); from 2.95 to 3.05 (mt, 1H : ArCH of isopropyl); 2.99 (dd, J = 14 and 6.5 Hz, 1H : 1H of CH_2 at position 4β); from 3.15 to 3.30 (mt, 3H : the other H of CH_2 at position 5β - the

other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.20 (s, 3H : NCH_3); 3.49 (mt, 1H : the other H of CH_2 at position 3δ); 3.93 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.60 (dd, J = 7.5 and 6 Hz, 1H : CH at position 3α); 4.79 (mt, 1H : CH at position 2α); 4.88 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.32 (dd, J = 9 and 6.5 Hz, 1H : CH at position 4α); from 5.40 to 5.50 (mt, 2H : CH at position 5α and the other H of CH_2 at position 5ε); 5.64 (d, J = 8 Hz, 1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.39 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.60 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.85 (d, J = 8 Hz, 2H : aromatic H at position 4δ); 6.99 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); from 7.20 to 7.40 (mt : the 8H corresponding to the 5 aromatic H at position 6α - to the aromatic H at position γ with respect to N - to 1' H_5 and to 1' H_4); 7.85 (broad d, J = 4 Hz, 1H : 1' H_6); 8.44 (d, J = 10 Hz, 1H : CONH at position 1); 8.69 (d, J = 8 Hz, 1H : CONH at position 6); 11.66 (s, 1H : OH).

1-(3-Methyl-2-oxobutyl)pyridinium bromide may be prepared as described by J.P. SAXENA, J. Indian Chem. Soc., 68, 99-100 (1991).

Example 36

By carrying out the process as in Example 5 but starting with 1.5 litres of acetonitrile, 100 g of 5δ-methylenepristinamycin I_A, 27.1 g of 1-(3-chloro-2-oxopropyl)pyridinium chloride, 88 g of ammonium

acetate and 5 hours reflux, a solid is obtained which is purified by two successive chromatographies on 1.5 kg and 100 g of silica (eluent: methylene chloride-methanol 97/3 by volume). The fractions containing the expected product are concentrated to give a solid which is purified by HPLC on 450 g of 10 µm C_8 silica (eluent: water-acetonitrile 70/30 by volume, containing 0.1% trifluoroacetic acid). The fractions are combined, the acetonitrile removed at 40°C under reduced pressure (2.7 kPa) and the pH of the aqueous phase adjusted to 8 by addition of water saturated with sodium bicarbonate. The aqueous phase is extracted with twice 50 cm^3 of methylene chloride. The organic phases are pooled, dried over sodium sulphate, filtered, concentrated under reduced pressure (45°C, 2.7 kPa) and the solid obtained is taken up in 20 cm^3 of diethyl ether. After filtration and then drying at 40°C under reduced pressure (90 Pa), 0.5 g of 2"-acetoxymethylpyrido[2,3-5γ,5δ]pristinamycin I_E is obtained in the form of a cream-coloured solid melting at 206°C.

Hz ^{1}H NMR spectrum (400 MHz, $CDCl_3$): 0.91 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); 1.25 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.30 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.58 (mt, 1H : the other H of CH_2 at position 3γ); from 1.60 to 1.85 (mts : the 3H corresponding to the CH_2 at position 2β and to 1H of CH_2 at position 5β); 2.03 (mt, 1H : the other H of CH_2 at position 3β); 2.14 (s, 3H :

$OCOCH_3$); Hz2.84 (s, 6H : $ArN(CH_3)_2$); 2.96 (dd, J = 13 and 5.5 Hz, 1H : 1H of CH_2 at position 4β); 3.14 (d, J = 16.5 Hz, 1H : the other H of CH_2 at position 5β); from 3.15 to 3.30 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.22 (s, 3H : NCH_3); 3.49 (mt, 1H : the other H of CH_2 at position 3δ); 3.93 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.60 (dd, J = 8 and 5.5 Hz, 1H : CH at position 3α); 4.79 (mt, 1H : CH at position 2α); 4.88 (dd, J = 10 and 1 Hz, 1H : CH at position 1α); 5.07 and 5.18 (2d, J = 13 Hz, 1H each : $ArCH_2OCO$); from 5.15 to 5.25 (mt, 1H : CH at position 4α); 5.40 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.45 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.60 (d, J = 8 Hz, 1H : CH at position 6α); 5.88 (split q, J Hz= 7 and 1 Hz, 1H : CH at position 1β); 6.34 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.56 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.85 (d, J = 8 Hz, 2H : aromatic H at position 4δ); 7.15 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); from 7.20 to 7.35 (mt : the 5H corresponding to aromatic H at position 6α); 7.36 (d, J = 8 Hz, 1H : aromatic H at position γ with respect to N); 7.40 (mt, 2H : 1' H_5 and 1' H_4); 7.89 (mt, 1H : 1'H_6); 8.40 (d, J = 10 Hz, 1H : CONH at position 1); 8.68 (d, J = 8 Hz, 1H : CONH at position 6); 11.65 (s, 1H : OH).

Example 37

When carrying out the procedure as in Example

20 but starting with 40 cm^3 of acetonitrile, 2 g of 2"-chloromethylpyrido[2,3-5γ,5δ]pristinamycin I_E, 1.5 cm^3 of cyclopropylamine and 0.34 g of potassium iodide, after refluxing for 24 hours 2.2 g of a foam are obtained, which foam is purified by two successive chromatographies on 60 g of silica (eluent: methylene chloride-methanol 95/5 by volume). The fractions are combined, dried over sodium sulphate, filtered and concentrated at 40°C under reduced pressure (2.7 kPa); the foam obtained is disintegrated in 30 cm^3 of diethyl ether. After filtration and drying at 40°C under reduced pressure (90 Pa), 0.55 g of 2"-cyclopropylaminomethylpyrido[2,3-5γ,5δ]pristinamycin I_E is obtained in the form of a yellow solid melting at 184°C.

^1H NMR spectrum (400 MHz, $CDCl_3$): from 0.35 to 0.50 (mt, 4H : CH_2CH_2 of cyclopropane); 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); 1.26 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.30 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.58 (mt, 1H : the other H of CH_2 at position 3γ); from 1.60 to 1.85 (mt : the 2H corresponding to the CH_2 at position 2β); 1.78 (dd, J = 16 and 6.5 Hz, 1H : 1H of CH_2 at position 5β); 2.03 (mt, 1H : the other H of CH_2 at position 3β); 2.16 (mt, 1H : CH of cyclopropane); 2.86 (s, 6H : $ArN(CH_3)_2$); 2.97 (dd, J = 13.5 and 6 Hz, 1H : 1H of CH_2 at position 4β); from 3.15 to 3.30 (mt, 2H : the other H of CH_2 at position 4β - the other H of CH_2 at position

5β and 1H of CH_2 at position 3δ); 3.22 (s, 3H : NCH_3); 3.49 (mt, 1H : the other H of CH_2 at position 3δ); 3.88 (s, 2H : $ArCH_2N$); 3.94 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.60 (dd, J = 8 and 5.5 Hz, 1H : CH at position 3α); 4.79 (mt, 1H : CH at position 2α); 4.88 (dd, J = 10 and 1 Hz, 1H : CH at position 1α); 5.26 (dd, J = 10 and 6 Hz, 1H : CH at position 4α); from 5.40 to 5.50 (mt, 2H : CH at position 5α and the other H of CH_2 at position 5ε); 5.62 (d, J = 8 Hz, 1H : CH at position 6α); 5.88 (split q, J = 7 and 1 Hz, 1H : CH at position 1β); 6.36 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.57 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.85 (d, J = 8 Hz, 2H : aromatic H at position 4δ); 7.10 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); from 7.20 to 7.35 (mt : the 6H corresponding to the 5 aromatic H at position 6α and to the aromatic H at position γ with respect to N); 7.39 (limiting AB, 2H : 1' H_5 and 1' H_4); 7.87 (dd, J = 4 and 2 Hz, 1H : 1' H_6); 8.42 (d, J = 10 Hz, 1H : CONH at position 1); 8.67 (d, J = 8 Hz, 1H : CONH at position 6); 11.65 (unresolved complex 1H : OH).

Example 38

By carrying out the procedure as in Example 20 but starting with 1.5 g of 2"-chloromethyl-pyrido[2,3-5γ,5δ]pristinamycin I_E in 30 cm^3 of acetonitrile, 0.5 cm^3 of diethylamine, 0.26 g of potassium iodide and after refluxing for 6 hours at 45°C, 1.35 g of product are obtained, which product is

purified by HPLC on 450 g of 10 µm C_8 silica (eluent: water-acetonitrile 60/40 by volume, containing 0.1% trifluoroacetic acid). The fractions are combined and the acetonitrile removed at 40°C under reduced pressure (2.7 kPa). The aqueous phase is adjusted to pH 8 by addition of water saturated with sodium bicarbonate and then extracted with 300 cm^3 of ethyl acetate. The organic phase is decanted off, dried over sodium sulphate, filtered and then concentrated under reduced pressure (45°C, 2.7 kPa) to give a solid which is crystallized from 30 cm^3 of methanol. After filtration, washing with 50 cm^3 of diisopropyl ether and drying at 40°C under reduced pressure (90 Pa), 0.4 g of 2"-N-diethylaminomethylpyrido[2,3-5γ,5δ]pristinamycin I_E is obtained in the form of a cottony white solid melting at 264°C.

^1H NMR spectrum (400 MHz, $CDCl_3$): 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); 1.04 (t, J = 7 Hz, 6H : CH_3 of diethylamino); from 1.20 to 1.35 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.30 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.58 (mt, 1H : the other H of CH_2 at position 3γ); from 1.60 to 1.80 (mt : the 2H corresponding to CH_2 at position 2β); 1.85 (dd, J = 16.5 and 5.5 Hz, 1H : 1H of CH_2 at position 5β); 2.03 (mt, 1H : the other H of CH_2 at position 3β); 2.55 (q, J = 7 Hz, 4H : the 2 NCH_2 of diethylamino); 2.85 (s, 6H : $ArN(CH_3)_2$); 2.98 (dd, J = 14 and 6 Hz, 1H : 1H of CH_2 at position 4β); from 3.15

to 3.30 (mt, 3H : the other H of CH_2 at position 4β - the other H of CH_2 $_{Hz}$at position 5β and 1H of CH_2 at position 3δ); 3.21 (s, 3H : NCH_3); 3.50 (mt, 1H : the other H of CH_2 at position 3δ); 3.66 (s, 2H : $ArCH_2N$); 3.94 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.60 (dd, J = 7.5 and 5.5 Hz, 1H : CH at position 3α); 4.79 (mt, 1H : CH at position 2α); 4.88 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.30 (dd, J = 9 and 6 Hz, 1H : CH at position 4α); 5.42 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.43 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.64 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.37 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.58 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.85 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.40 (mt : the 9H corresponding to the 5 aromatic H at position 6α - to the aromatic H at position β with respect to N - to the aromatic H at position γ with respect to N - to 1' H_4 and to 1' H_5); 7.85 (broad d, J = 4 Hz, 1H : 1' H_6); 8.43 (d, J = 10 Hz, 1H : CONH at position 1); 8.68 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.65 (broad s, 1H : OH).

2"-Chloromethylpyrido[2,3-5γ,5δ]pristinamycin I_E may be obtained as described in Example 10.

Example 39

By carrying out the procedure as in Example 6 but starting with 5.6 g of 5δ-methylenevirginiamycin S

in 100 cm^3 of acetonitrile, 1.15 g of 1-acetonyl-pyridinium chloride, 5.17 g of ammonium acetate and heating for 4 hours under reflux, a red oil is obtained which is chromatographed on 500 g of silica (eluent: methylene chloride-methanol 98/2 by volume) to give 2.1 g of yellow foam. The latter is purified by HPLC on 450 g of 10 µm C_8 silica (eluent: water-acetonitrile 65/35 by volume, containing 0.1% trifluoroacetic acid). The fractions are combined, the acetonitrile removed at 40°C under reduced pressure (2.7 kPa), the pH of the aqueous phase adjusted to 7 by addition of water saturated with sodium bicarbonate; the precipitate obtained is filtered, washed with 20 cm^3 of water and then 20 cm^3 of diethyl ether. After filtration and drying at 40°C under reduced pressure (90 Pa), 0.39 g of 2"-methylpyrido[2,3-5γ,5δ]-5γ-deoxyvirginiamycin S is obtained in the form of a white solid melting at 176°C.

5δ-methylenevirginiamycin S may be obtained as described.

^1H NMR spectrum (400 MHz, $CDCl_3$): 0.93 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); 1.27 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); from 1.50 to 1.85 (mt : the 4H corresponding to the other H of CH_2 at position 3γ - to the CH_2 at position 2β and 1H of CH_2 at position 5β); 2.04 (mt, 1H : the other H of CH_2 at position 3β); 2.50 (s, 3H : $ArCH_3$); 3.07 (dd, J = 13 and

6 Hz, 1H : 1H of CH_2 at position 4β); from 3.15 to 3.35 (mt, 3H : the other H of CH_2 at position 4β - the other H of CH_2 at position 5β and 1H of CH_2 at position 3δ); 3.22 (s, 3H : NCH_3); 3.51 (mt, 1H : the other H of CH_2 at position 3δ); 3.92 (d, J = 17.5 Hz, 1H : 1H of CH_2 at position 5ε); 4.58 (dd, J = 8 and 6.5 Hz, 1H : CH at position 3α); 4.80 (mt, 1H : CH at position 2α); 4.87 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.34 (dd, J = 10 and 6 Hz, 1H : CH at position 4α); from 5.35 to 5.45 (mt, 2H : the other H of CH_2 at position 5ε and CH at position 5α); 5.64 (d, J = 8 Hz, 1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.56 (d, J = 9.5 Hz, 1H : CONH at position 2); from 6.95 to 7.40 (mt : the 13H corresponding to the 5 aromatic H at position 6α - to the 5 aromatic H at position 4β - to the aromatic H at position γ with respect to N - to 1' H_4 and to 1' H_5); 6.96 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); 7.81 (broad d, J = 4 Hz, 1H : 1' H_6); 8.42 (d, J = 10 Hz, 1H : CONH at position 1); 8.64 (d, J = 8 Hz, 1H : CONH at position 6); 11.65 (s, 1H : OH).

Example 40

By carrying out the procedure by analogy with Example 15 but starting with 4ε-chloro-5δ-methylene-pristinamycin I_A, 4ε-chloro-2"-(2-pyridyl)pyrido[2,3-5γ,5δ]pristinamycin I_E is obtained in the form of a white solid melting at 194°C.

^1H NMR spectrum (400 MHz, $CDCl_3$): 0.93 (t, J =

7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.35 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.58 (mt, 1H : the other H of CH_2 at position 3γ); from 1.60 to 1.85 (mt, the 3H corresponding to the CH_2 at position 2β and to 1H of CH_2 at position 5β); 2.04 (mt, 1H : the other H of CH_2 at position 3β); 2.56 (s, 6H : $ArN(CH_3)_2$); 2.99 (dd, J = 13 and 5.5 Hz, 1H : 1H of CH_2 at position 4β); from 3.20 to 3.35 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.23 (s, 3H : NCH_3); 3.36 (d, J = 16.5 Hz, 1H : the other H of CH_2 at position 5β); 3.51 (mt, 1H : the other HzH of CH_2 at position 3δ); 4.01 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.60 (dd, J = 7.5 and 6 Hz, 1H : CH at position 3α); 4.81 (mt, 1H : CH at position 2α); 4.91 (dd, J = 10 and 1 Hz, 1H : CH at position 1α); 5.26 (dd, J = 10 and 5.5 Hz, 1H : CH at position 4α); 5.46 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.53 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.63 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.89 (split q, J = 7 and 1 Hz, 1H : CH at position 1β); 6.47 (d, J = 8 Hz, 1H : aromatic H at position 4ε); 6.57 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.77 (dd, J = 8 and 2 Hz, 1H : aromatic H at position 4δ at the para position with respect to the Cl); 7.13 (d, J = 2 Hz, 1H : aromatic H at position 4δ at the ortho position with respect to the Cl); from 7.20 to 7.40 (mt : the 6H corresponding to the 5 aromatic H at

position 6α and to H_5 of pyridine); 7.41 (broad d, J = 8 Hz, 1H : 1' H_4); 7.50 (d, J = 8 Hz, 1H : aromatic H at position γ with respect to N); 7.53 (dd, J = 8 and 4.5 Hz, 1H : 1' H_5); 7.74 (split t, J = 8 and 1.5 Hz, 1H : H_4 of pyridine); 7.90 (broad d, J = 4.5 Hz, 1H : 1' H_6); 8.24 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); 8.37 (d, J = 8 Hz, 1H : H_3 of pyridine); 8.38 (d, J = 10 Hz, 1H : CONH at position 1); 8.64 (d, J = 8.5 Hz, 1H : CONH at position 6); 8.67 (broad d, J = 4.5 Hz, 1H : H_6 of pyridine); 11.67 (s, 1H : OH).

Example 41

By carrying out the procedure by analogy with Example 18 but starting with 4ε-chloro-5δ-methylene-pristinamycin I_A, 4ε-chloro-2"-(2-pyridyl)pyrido[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E is obtained in the form of a white solid melting at 204°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$): 0.93 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); 1.27 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.59 (mt, 1H : the other H of CH_2 at position 3γ); 1.67 and 1.75 (2 mts, 1H each : CH_2 at position 2β); 1.84 (dd, J = 16.5 and 6 Hz, 1H : 1H of CH_2 at position 5β); 2.04 (mt, 1H : the other H of CH_2 at position 3β); 2.53 (s, 3H : $ArNCH_3$); 2.94 (dd, J = 13.5 and 6 Hz, 1H : 1H of CH_2 at position 4β); from 3.15 to 3.30 (mt, 2H : the other H

of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.22 (s, 3H : NCH_3); 3.35 (d, J = 16.5 Hz, 1H : the other H of CH_2 at position 5β); 3.49 (mt, 1H : the other H of CH_2 at position 3δ); 4.00 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.60 (dd, J = 8 and 7 Hz, 1H : CH at position 3α); 4.79 (mt, 1H : CH at position 2α); 4.89 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.19 (dd, J = 10 and 6 Hz, 1H : CH at position 4α); from 5.45 to 5.55 (mt, 2H : CH at position 5α and the other H of CH_2 at position 5ε); 5.64 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.09 (d, J = 8 Hz, 1H : aromatic H at position 4ε); 6.57 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.75 (broad d, J = 8 Hz, 1H : aromatic H at position 4δ at the para position with respect to the Cl); 6.95 (broad s, 1H : aromatic H at position 4δ at the ortho position with respect to the Cl); from 7.20 to 7.40 (mt : the 6H corresponding to the 5 aromatic H at position 6α and to H_5 of pyridine); 7.41 (broad d, J = 8 Hz, 1H : 1' H_4); 7.48 (d, J = 8 Hz, 1H : aromatic H at position γ with respect to N); 7.51 (dd, J = 8 and 4 Hz, 1H : 1' H_5); 7.77 (broad t, J = 8 Hz, 1H : H_4 of pyridine); 7.97 (broad d, J = 4 Hz, 1H : 1' H_6); 8.19 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); from 8.35 to 8.45 (mt, 2H : H_3 of pyridine and CONH at position 1); 8.63 (d, J = 8.5 Hz, 1H : CONH at position 6); 8.67 (broad d, J = 4.5 Hz, 1H : H_6 of pyridine); 11.67 (s, 1H : OH).

Example 42

By carrying out the procedure by analogy with Example 7 but starting with 4ε-chloro-5δ-methylene-pristinamycin I_A, 4ε-chloro-2"-ethylpyrido[2,3-5γ,5δ]pristinamycin I_E is obtained in the form of a white solid melting at 184°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$): 0.91 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.27 (t, J = 7.5 Hz, 3H : CH_3 of ethyl); 1.30 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.59 (mt, 1H : the other H of CH_2 at position 3γ); 1.67 and 1.75 (2 mts, 1H each : CH_2 at position 2β); 1.90 (dd, J = 16 and 5.5 Hz, 1H : 1H of CH_2 at position 5β); 2.04 (mt, 1H : the other H of CH_2 at position 3β); 2.72 (s, 6H : $ArN(CH_3)_2$); 2.77 (mt, 2H : $ArCH_2$ of ethyl); 3.01 (dd, J = 14 and 7 Hz, 1H : 1H of CH_2 at position 4β); from 3.15 to 3.25 (mt, 2H : the other H of CH_2 at position 4β); 3.19 (s, 3H : NCH_3); from 3.25 to 3.35 (mt, 1H : 1H of CH_2 at position 3δ); 3.33 (d, J = 16 Hz, 1H : the other H of CH_2 at position 5β); 3.51 (mt, 1H : the other H of CH_2 at position 3δ); 3.95 (d, J = 17.5 Hz, 1H : 1H of CH_2 at position 5ε); 4.57 (broad t, J = 6.5 Hz, 1H : CH at position 3α); 4.78 (mt, 1H : CH at position 2α); 4.89 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.34 (mt, 1H : CH at position 4α); 5.41 (d, J = 17.5 Hz, 1H : the other H of CH_2 at position 5ε); 5.47 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.61 (d, J = 8.5 Hz,

1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.59 (mt, 2H : aromatic H at position 4ε and CONH at position 2); 6.79 (broad d, J = 8 Hz, 1H : aromatic H at position 4δ at the para position with respect to the Cl); 6.98 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); 7.06 (broad s, 1H : aromatic H at position 4δ at the ortho position with respect to the Cl); from 7.20 to 7.40 (mt : the 8H corresponding to the 5 aromatic H at position 6α - to the aromatic H at position γ with respect to N - to 1' H_4 and to 1' H_5); 7.82 (broad d, J = 4 Hz, 1H : 1' H_6); 8.38 (d, J = 10 Hz, 1H : CONH at position 1); 8.64 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.67 (s, 1H : OH).

Example 43

By carrying out the procedure by analogy with Example 17 but starting with 4ε-chloro-5δ-methylene-pristinamycin I_A, 4ε-chloro-2"-ethylpyrido[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E is obtained in the form of a white solid melting at 186°C.

^1H NMR spectrum (400 MHz, $CDCl_3$): 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.35 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.28 (t, J = 7.5 Hz, 3H : CH_3 of ethyl); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.58 (mt, 1H : the other H of CH_2 at position 3γ); from 1.60 to 1.85 (mt : the 2H corresponding to the CH_2 at position 2β); 1.93

(dd, J = 16 and 6 Hz, 1H : 1H of CH_2 at position 5β); 2.03 (mt, 1H : the other H of CH_2 at position 3β); 2.76 (mt, 2H : $ArCH_2$ of ethyl); 2.77 (s, 3H : $ArNCH_3$); 2.96 (dd, J = 14 and 6.5 Hz, 1H : 1H of CH_2 at position 4β); from 3.10 to 3.30 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.19 (s, 3H : NCH_3); 3.30 (d, J = 16 Hz, 1H : the other H of CH_2 at position 5β); 3.50 (mt, 1H : the other H of CH_2 at position 3δ); 3.95 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.21 (unresolved complex, 1H : ArNH); 4.60 (dd, J = 7.5 and 5.5 Hz, 1H : CH at position 3α); 4.79 (mt, 1H : CH at position 2α); 4.88 (dd, J = 10 and 1 Hz, 1H : CH at position 1α); 5.28 (dd, J = 9 and 6.5 Hz, 1H : CH at position 4α); 5.42 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.46 (broad d, J = 6 Hz, 1H : CH at position 5α); 5.63 (d, J = 8 Hz, 1H : CH at position 6α); 5.89 (split q, J = 7 and 1 Hz, 1H : CH at position 1β); 6.19 (d, J = 8 Hz, 1H : aromatic H at position 4ε); 6.57 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.77 (dd, J = 8 and 1.5 Hz, 1H : aromatic H at position 4δ at the para position with respect to the Cl); 6.94 (d, J = 1.5 Hz, 1H : aromatic H at position 4δ at the para position with respect to the Cl); 6.98 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); from 7.20 to 7.45 (mt : the 6H corresponding to the 5 aromatic H at position 6α and to the aromatic H at position γ with respect to N); 7.37 (limiting AB, 2H : 1' H_4 and 1' H_5); 7.84 (dd, J = 4 and

1.5 Hz, 1H : 1' H_6); 8.40 (d, J = 10 Hz, 1H : CONH at position 1); 8.67 (d, J = 8 Hz, 1H : CONH at position 6); 11.66 (s, 1H : OH).

Example 44

By carrying out the procedure by analogy with Example 6 but starting with 4ε-chloro-5δ-methylene-pristinamycin I_A, 4ε-chloro-2"-methylpyrido[2,3-5γ,5δ]pristinamycin I_E is obtained in the form of a yellow powder melting at 210°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$): 0.93 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.40 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.29 (d, J = 7 Hz, 3H : CH_3 at position 1γ); from 1.50 to 1.80 (mt : the 3H corresponding to the other H of CH_2 at position 3γ and to CH_2 at position 2β); 1.81 (dd, J = 16 and 5.5 Hz, 1H : 1H of CH_2 at position 5β); 2.04 (mt, 1H : the other H of CH_2 at position 3β); 2.48 (s, 3H : $ArCH_3$); 2.74 (s, 6H : $ArN(CH_3)_2$); 3.02 (dd, J = 14 and 6.5 Hz, 1H : 1H of CH_2 at position 4β); from 3.15 to 3.30 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.20 (s, 3H : NCH_3); 3.28 (d, J = 16 Hz, 1H : the other H of CH_2 at position 5β); 3.51 (mt, 1H : the other H of CH_2 at position 3δ); 3.96 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.59 (dd, J = 7.5 and 7 Hz, 1H : CH at position 3α); 4.80 (mt, 1H : CH at position 2α); 4.90 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.31 (dd, J = 9 and 6.5 Hz, 1H : CH at position 4α); 5.40 (d, J = 17 Hz, 1H : the other H of

CH_2 at position 5ε); 5.47 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.61 (d, J = 8 Hz, 1H : CH at position 6α); 5.89 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.45 (d, J = 8 Hz, 1H : aromatic H at position 4ε); 6.59 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.80 (broad d, J = 8 Hz, 1H : aromatic H at position 4δ at the para position with respect to the Cl); 6.97 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); 7.10 (broad s, 1H : aromatic H at position 4δ at the ortho position with respect to the Cl); from 7.20 to 7.35 (mt : the 6H corresponding to the 5 aromatic H at position 6α and to the aromatic H at position γ with respect to N); 7.37 (broad d, J = 8 Hz, 1H : 1' H_4); 7.42 (dd, J = 8 and 4.5 Hz, 1H : 1' H_5); 7.84 (broad d, J = 4.5 Hz, 1H : 1' H_6); 8.37 (d, J = 10 Hz, 1H : CONH at position 1); 8.61 (d, J = 8 Hz, 1H : CONH at position 6); 11.68 (s, 1H : OH).

Example 45

4 g of 2"-hydroxymethylpyrido[2,3-5γ,5δ]pristinamycin I_E and 0.48 g of selenium oxide are introduced into a three-necked flask containing 70 cm^3 of dioxane and the mixture is refluxed for 1 hour. The reaction mixture is filtered on Celite® and the filtrate concentrated under reduced pressure at 45°C (2.7 kPa) to give 5.7 g of a chestnut-coloured foam which is purified by 2 successive chromatographies on 60 g of silica (eluent: methylene chloride-methanol 97/3 by volume). The fractions are combined and

concentrated under reduced pressure at 45°C (2.7 kPa). The solid obtained is stirred in 30 cm^3 of diethyl ether, filtered and dried at 40°C under reduced pressure (90 Pa) to give 0.76 g of 2"-formylpyrido[2,3-5γ,5δ]pristinamycin I_E in the form of a white solid melting at 202°C.

^1H NMR spectrum (400 MHz, $CDCl_3$): 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.35 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); from 1.50 to 1.75 (mt : the 3H corresponding to the other H of CH_2 at position 3γ - to 1H of CH_2 at position 2β and to 1H of CH_2 at position 5β); 1.74 (mt, 1H : the other H of CH_2 at position 2β); 2.05 (mt, 1H : the other H of CH_2 at position 3β); 2.79 (s, 6H : $ArN(CH_3)_2$); 2.95 (dd, J = 13 and 5 Hz, 1H : 1H of CH_2 at position 4β); from 3.15 to 3.30 (mt, 3H : the other H of CH_2 at position 4β - the other H of CH_2 at position 5β and 1H of CH_2 at position 3δ); 3.26 (s, 3H : NCH_3); 3.50 (mt, 1H : the other H of CH_2 at position 3δ); 3.97 (d, J = 18 Hz, 1H : 1H of CH_2 at position 5ε); 4.62 (dd, J = 7.5 and 6 Hz, 1H : CH at position 3α); 4.81 (mt, 1H : CH at position 2α); 4.89 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.14 (dd, J = 11 and 5 Hz, 1H : CH at position 4α); 5.44 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.52 (d, J = 18 Hz, 1H : the other H of CH_2 at position 5ε); 5.62 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.29 (d, J

= 8 Hz, 2H : aromatic H at position 4ε); 6.56 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.86 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.40 (mt : the 5H corresponding to the aromatic H at position 6α); 7.45 (broad d, J = 8 Hz, 1H : 1' H_4); from 7.45 to 7.55 (mt, 2H : 1' H_5 and aromatic H at position γ with respect to N); 7.77 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); 8.00 (broad d, J = 4 Hz, 1H : 1' H_6); 8.40 (d, J = 10 Hz, 1H : CONH at position 1); 8.69 (d, J = 8.5 Hz, 1H : CONH at position 6); 9.97 (s, 1H : COH); 11.65 (s, 1H : OH).

2"-hydroxymethylpyrido[2,3-5γ,5δ]-pristinamycin I_E may be obtained as described in Example 11.

Example 46

1.7 g of 2"-formylpyrido[2,3-5γ,5δ]-pristinamycin I_E and 1.4 g of ammonium acetate are introduced into a three-necked flask containing 100 cm^3 of dioxane and the mixture is refluxed for 1 hour. The reaction mixture is concentrated under reduced pressure and then taken up in 100 cm^3 of water and 100 cm^3 of methylene chloride. After decantation, drying of the organic phase over sodium sulphate, filtration and concentration to dryness, 1.5 g of a solid is obtained which is chromatographed on 60 g of silica (eluent: methylene chloride-methanol 97/3 by volume). The fractions are combined and then concentrated under reduced pressure at 45°C (2.7 kPa). The solid obtained

is taken up in 30 cm^3 of diethyl ether and then filtered and dried at 40°C under reduced pressure (90 Pa) to give 0.32 g of 2"-carbamoylpyrido[2,3-5γ,5δ]-pristinamycin I_E in the form of an orange-coloured solid melting at 226°C.

^1H NMR spectrum (400 MHz, $CDCl_3$): 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); 1.26 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.30 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.43 (dd, J = 16.5 and 5.5 Hz, 1H : 1H of CH_2 at position 5β); from 1.50 to 1.70 (mt : the 2H corresponding to the other H of CH_2 at position 3γ and to 1H of CH_2 at position 2β); 1.75 (mt, 1H : the other H of CH_2 at position 2β); 2.06 (mt, 1H : the other H of CH_2 at position 3β); 2.79 (s, 6H : $ArN(CH_3)_2$); 2.93 (dd, J = 12.5 and 4.5 Hz, 1H : 1H of CH_2 at position 4β); 3.08 (d, J = 16.5 Hz, 1H : the other H of CH_2 at position 5β); from 3.15 to 3.30 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.26 (s, 3H : NCH_3); 3.49 (mt, 1H : the other H of CH_2 at position 3δ); 3.94 (d, J = 17.5 Hz, 1H : 1H of CH_2 at position 5ε); 4.62 (dd, J = 8 and 6.5 Hz, 1H : CH at position 3α); 4.81 (mt, 1H : CH at position 2α); 4.89 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.09 (dd, J = 11.5 and 4.5 Hz, 1H : CH at position 4α); 5.39 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.48 (d, J = 5 Hz, 1H : 1H of $CONH_2$); 5.51 (d, J = 17.5 Hz, 1H : the other H of CH_2 at position 5ε); 5.60 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.88 (broad q,

J = 7 Hz, 1H : CH at position 1β); 6.28 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.57 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.87 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.40 (mt : the 5H corresponding to the aromatic H at position 6α); 7.46 (broad d, J = 8 Hz, 1H : 1' H_4); from 7.50 to 7.60 (mt, 2H : 1' H_5 and aromatic H at position γ with respect to N); 7.78 (d, J = 5 Hz, 1H : the other H of $CONH_2$); 7.99 (mt, 1H : 1'H_6); 8.00 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); 8.38 (d, J = 10 Hz, 1H : CONH at position 1); 8.67 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.67 (s, 1H : OH).

2"-formylpyrido[2,3-5γ,5δ]pristinamycin I_E may be obtained as described in Example 45.

Example 47

By carrying out the procedure as in Example 22 but starting with 40 cm^3 of acetonitrile, 4.6 g of 5δ-dimethylaminomethylenepristinamycin I_A, 0.38 g of acetamidine and heating for 12 hours at 60°C, a solid which is chromatographed on 400 g of silica (eluent: methylene chloride-methanol 97/3 by volume) is obtained after concentrating the reaction mixture to dryness at 45°C (2.7 kPa). The fractions are pooled, dried over sodium sulphate, filtered and concentrated at 45°C under reduced pressure (2.7 kPa). The solid obtained is crystallized from 10 cm^3 of methanol and then filtered and dried at 40°C (90 Pa) to give 0.4 g of 2"-methylpyrimido[4,5-5γ,5δ]pristinamycin I_E in the form of

white crystals melting at 265°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$ with addition of $(CD_3)_2SO$ d6) : 0.79 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.05 to 1.20 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.14 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.24 (dd, J = 17 and 5.5 Hz, 1H : 1H of CH_2 at position 5β); 1.46 (mt, 1H : the other H of CH_2 at position 3γ); 1.52 and 1.62 (2 mts, 1H each : CH_2 at position 2β); 1.95 (mt, 1H : the other H of CH_2 at position 3β); 2.51 (s, 3H : $ArCH_3$); 2.74 (s, 6H : $ArN(CH_3)_2$); from 2.75 to 2.85 (mt, 1H : 1H of CH_2 at position 4β); 2.83 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5β); from 3.05 to 3.20 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.13 (s, 3H : NCH_3); 3.37 (mt, 1H : the other H of CH_2 at position 3δ); 3.70 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.48 (dd, J = 8 and 6 Hz, 1H : CH at position 3α); 4.65 (mt, 1H : CH at position 2α); 4.75 (broad d, J = 10 Hz, 1H : CH at position 1α); 4.94 (dd, J = 11.5 and 5 Hz, 1H : CH at position 4α); 5.24 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.30 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.45 (d, J = 8 Hz, 1H : CH at position 6α); 5.72 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.20 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.54 (d, J = 9.5 Hz, 1H : CONH at position 2); 6.72 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.05 to 7.30 (mt : the 5H corresponding to the aromatic H at position 6α);

7.32 (broad d, J = 8 Hz, 1H : 1' H_4); 7.37 (dd, J = 8 and 4 Hz, 1H : 1' H_5); 7.81 (broad d, J = 4 Hz, 1H : 1' H_6); 8.17 (s, 1H : CH=N); 8.22 (d, J = 10 Hz, 1H : CONH at position 1); 8.56 (d, J = 8 Hz, 1H : CONH at position 6); 11.52 (s, 1H : OH).

Example 48

By carrying out the procedure as in Example 22 but starting with 40 cm^3 of dimethylformamide, 1.84 g of 5δ-dimethylaminomethylenepristinamycin I_A, 0.41 g of 2-pyrazinecarboxamidine hydrochloride and 1 cm^3 of diisopropylamine, the reaction mixture is heated for 12 hours at 65°C. 0.16 g of 2-pyrazinecarboxamidine hydrochloride is added and the heating is continued for an additional 24 hours. After treating and concentrating the reaction mixture to dryness at 45°C (2.7 kPa), 2.1 g of solid are obtained, which solid is chromatographed on 100 g of silica (eluent: methylene chloride-methanol 97/3 by volume). The fractions are pooled, dried over sodium sulphate, filtered and concentrated at 45°C under reduced pressure (2.7 kPa). The solid obtained is crystallized from 10 cm^3 of methanol, filtered, washed with twice 5 cm^3 of diisopropyl ether and then dried at 40°C (90 Pa) to give 0.49 g of 2"-(2-pyrazinyl)pyrimido[4,5-5γ,5δ]pristinamycin I_E in the form of yellow crystals melting at 254°C.

^1H NMR spectrum (400 MHz, $CDCl_3$) : 0.93 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.25 to 1.40

(mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.51 (dd, J = 17 and 6 Hz, 1H : 1H of CH_2 at position 5β); from 1.55 to 1.65 (mt, 1H corresponding to the other H of CH_2 at position 3γ); 1.67 and 1.75 (2 mts, 1H each : CH_2 at position 2β); 2.08 (mt, 1H : the other H of CH_2 at position 3β); 2.64 (s, 6H : $ArN(CH_3)_2$); 2.94 (dd, J = 12 and 5 Hz, 1H : 1H of CH_2 at position 4β); 3.18 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5β); from 3.20 to 3.35 (mt, 1H : 1H of CH_2 at position 3δ and the other H of CH_2 at position 4β); 3.26 (s, 3H : NCH_3); 3.51 (mt, 1H : the other H of CH_2 at position 3δ); 3.90 (d, J = 17.5 Hz, 1H : 1H of CH_2 at position 5ε); 4.61 (dd, J = 8 and 6 Hz, 1H : CH at position 3α); 4.81 (mt, 1H : CH at position 2α); 4.90 (dd, J = 10 and 1 Hz, 1H : CH at position 1α); 5.12 (dd, J = 12 and 5 Hz, 1H : CH at position 4α); 5.45 (broad d, J = 6 Hz, 1H : CH at position 5α); 5.53 (d, J = 17.5 Hz, 1H : the other H of CH_2 at position 5ε); 5.65 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.89 (split q, J = 7 and 1 Hz, 1H : CH at position 1β); 6.29 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.55 (d, J = 10 Hz, 1H : CONH at position 2); 6.87 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.40 (mt : the 5H corresponding to the aromatic H at position 6α); 7.48 (broad d, J = 8.5 Hz, 1H : 1' H_4); 7.53 (dd, J = 8.5 and 4 Hz, 1H : 1' H_5); 8.02 (broad d, J = 4 Hz, 1H : 1' H_6); 8.41 (d, J = 10 Hz, 1H : CONH at position 1);

8.58 (s, 1H : CH=N); 8.67 (d, J = 2 Hz, 1H : H at position 5 of pyrazine); 8.74 (d, J = 8.5 Hz, 1H : CONH at position 6); 8.77 (dd, J = 2 and 1.5 Hz, 1H : H at position 6 of pyrazine); 9.68 (d, J = 1.5 Hz, 1H : H at position 3 of pyrazine); 11.65 (s, 1H : OH).

Example 49

By carrying out the procedure as in Example 22 but starting with 40 cm^3 of dimethylformamide, 3 g of 5δ-dimethylaminomethylenepristinamycin I_A, 0.74 g of 1H-pyrozolecarboxamidine hydrochloride and 2 cm^3 of diisopropylethylamine, the reaction mixture is heated for 4 hours at 65°C. After treating and concentrating the reaction mixture to dryness at 45°C (2.7 kPa), 2.4 g of a solid is obtained which is chromatographed on 160 g of silica (eluent: methylene chloride-methanol 96/4 by volume). The fractions are combined, dried over sodium sulphate, filtered and concentrated at 45°C under reduced pressure (2.7 kPa). The foam obtained is crystallized from 10 cm^3 of isopropanol. After filtration, washing and drying at 40°C (90 Pa), 0.41 g of 2"-(1-pyrazolyl)pyrimido[4,5-5γ,5δ]pristinamycin I_E is obtained in the form of yellow crystals melting at 197°C.

^1H NMR spectrum (400 MHz, $CDCl_3$) : 0.93 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.35 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.45 (dd, J = 17 and 6 Hz, 1H : 1H of CH_2 at

position 5β); from 1.55 to 1.65 (mt, 1H corresponding to the other H of CH_2 at position 3γ); 1.67 and 1.75 (2 mts, 1H each : CH_2 at position 2β); 2.07 (mt, 1H : the other H of CH_2 at position 3β); 2.67 (s, 6H : $ArN(CH_3)_2$); 2.93 (dd, J = 12 and 4.5 Hz, 1H : 1H of CH_2 at position 4β); 3.10 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5β); from 3.15 to 3.30 (mt, 1H : 1H of CH_2 at position 3δ and the other H of CH_2 at position 4β); 3.27 (s, 3H : NCH_3); 3.51 (mt, 1H : the other H of CH_2 at position 3δ); 3.84 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.62 (dd, J = 8 and 6 Hz, 1H : CH at position 3α); 4.81 (mt, 1H : CH at position 2α); 4.89 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.07 (dd, J = 12 and 4.5 Hz, 1H : CH at position 4α); 5.41 (broad d, J = 6 Hz, 1H : CH at position 5α); 5.48 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.67 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.89 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.29 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.48 (broad d, J = 2 Hz, 1H : H at position 4 of pyrazole); 6.53 (d, J = 10 Hz, CONH at position 2); 6.87 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.40 (mt : the 5H corresponding to the aromatic H at position 6α); 7.48 (broad d, J = 8.5 Hz, 1H : 1' H_4); 7.53 (dd, J = 8.5 and 4 Hz, 1H : 1' H_5); 7.80 (broad s, 1H : H at position 3 of pyrozole); 8.00 (broad d, J = 4 Hz, 1H : 1' H_6); 8.38 (d, J = 10 Hz, 1H : CONH at position 1); 8.38 (s, 1H : CH=N); 8.54 (d, J = 2 Hz, 1H : H at position 5 of

pyrazole); 8.71 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.65 (s, 1H : OH).

Example 50

By carrying out the procedure as in Example 22 but starting with 40 cm^3 of dimethylformamide, 1.84 g of 5δ-dimethylaminomethylenepristinamycin I_A, 0.60 g of S-(2-morpholinoethyl)isothiouronium hydrochloride, 1 cm^3 of diisopropylamine and heating overnight at 65°C, 1.5 g of a yellow solid which is purified by two successive chromatographies with 100 g and 200 g of silica respectively (eluent: methylene chloride-methanol 97/3 by volume) are obtained after treating and concentrating the reaction mixture to dryness at 45°C (2.7 kPa). The fractions are pooled, dried over sodium sulphate, filtered and concentrated at 45°C under reduced pressure (2.7 kPa). The solid obtained is taken up in 10 cm^3 of diisopropyl ether. After filtration, washing and drying at 40°C (90 Pa), 0.51 g of 2"-(2-morpholinoethylthio)pyrimido[4,5-5γ,5δ]pristinamycin I_E is obtained in the form of an off-white solid melting at 187°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$) : 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.40 (mt, 3H : 1H of CH_2 at position 3β - 1H of CH_2 at position 3γ and 1H of CH_2 at position 5β); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); from 1.50 to 1.70 (mt : the 2H corresponding to the other H of CH_2 at position 3γ and to 1H of CH_2 at position 2β); 1.75 (mt, 1H : the

other H of CH_2 at position 2β); 2.04 (mt, 1H : the other H of CH_2 at position 3β); 2.53 (unresolved complex, 4H : the 2 NCH_2 of morpholine); 2.69 (t, J = 7.5 Hz, 2H : NCH_2); from 2.80 to 2.95 (mt, 2H : Hzthe other H of CH_2 at position 5β and 1H of CH_2 at position 4β); 2.90 (s, 6H : $ArN(CH_3)_2$); from 3.15 to 3.35 (mt, 4H : $ArSCH_2$ - the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.27 (s, 3H : NCH_3); 3.50 (mt, 1H : the other H of CH_2 at position 3δ); from 3.65 to 3.80 (mt, 5H : the 2 OCH_2 of morpholine and 1H of CH_2 at position 5ε); 4.60 (dd, J = 8 and 6 Hz, 1H : CH at position 3α); 4.80 (mt, 1H : CH at position 2α); 4.89 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.08 (dd, J = 11.5 and 5 Hz, 1H : CH at position 4α); 5.33 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.40 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.65 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.35 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.52 (d, J = 10 Hz, 1H : CONH at position 2); 6.85 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.15 to 7.40 (mt : the 5H corresponding to the aromatic H at position 6α); 7.45 (broad d, J = 8.5 Hz, 1H : 1' H_4); 7.49 (dd, J = 8.5 and 4 Hz, 1H : 1' H_5); 7.92 (broad d, J = 4 Hz, 1H : Hz1' H_6); 8.16 (s, 1H : CH=N); 8.37 (d, J = 10 Hz, 1H : CONH at position 1); 8.70 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.64 (s, 1H : OH).

S-(2-morpholinoethyl)isothiouronium

dihydrochloride may be prepared according to DOHERTY Chem. Soc., 79, 5667-70, (1957) or CLINTON J. Am. Chem. Soc., 70, 950, (1948).

Example 51

By carrying out the procedure as in Example 22 but starting with 50 cm^3 of dimethylformamide, 2 g of 5δ-dimethylaminomethylenepristinamycin I_A, 0.67 g of S-(4-pyridylmethyl)isothiouronium hydrochloride, 1.5 cm^3 of diisopropylamine and heating at 65°C for 48 hours, a solid which is chromatographed on 40 g of silica (eluent: methylene chloride-methanol 98/2 by volume) and then HPLC on 450 g of 10 µm C_8 silica (eluent: water-acetonitrile 72.5/27.5 by volume, containing 0.1% trifluoroacetic acid) is obtained after treating and concentrating the reaction mixture to dryness at 45°C (2.7 kPa). The fractions are combined, the acetonitrile removed at 40°C under reduced pressure (2.7 kPa) and then the pH of the aqueous phase is adjusted to 7-8 by addition of water saturated with sodium bicarbonate. The precipitate obtained is filtered, dried at 40°C under 90 Pa to give 0.22 g of 2"-(4-pyridylmethylthio)-pyrimido[4,5-5γ,5δ]pristinamycin I_E in the form of a white solid melting at 195°C.

^1H NMR spectrum (400 MHz, $CDCl_3$) : 0.91 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.40 (mt, 3H : 1H of CH_2 at position 3β - 1H of CH_2 at position 3γ and 1H of CH_2 at position 5β); 1.31 (d, J = 7 Hz, 3H : CH_3 at position 1γ); from 1.50 to 1.75 (mt :

the 2H corresponding to 1H of CH_2 at position 2β and the other H of CH_2 at position 3γ); 1.74 (mt, 1H : the other H of CH_2 at position 2β); 2.05 (mt, 1H : the other H of CH_2 at position 3β); 2.83 (s, 6H : $ArN(CH_3)_2$); from 2.90 to 3.00 (mt, 2H : 1H of CH_2 at position 4β and the other H of CH_2 at position 5β); from 3.15 to 3.30 (mt, 2H : 1H of CH_2 at position 3δ and the other H of CH_2 at position 4β); 3.26 (s, 3H : NCH_3); 3.50 (mt, 1H : the other H of CH_2 at position 3δ); 3.76 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.27 and 4.39 (2 d, J = 15 Hz, 1H each : $ArSCH_2Ar$); 4.61 (dd, J = 7.5 and 5.5 Hz, 1H : CH at position 3α); 4.79 (mt, 1H : CH at position 2α); 4.87 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.07 (dd, J = 12 and 4.5 Hz, 1H : CH at position 4α); 5.33 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.39 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.64 (d, J = 8 Hz, 1H : CH at position 6α); 5.87 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.33 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.53 (d, J = 10 Hz, 1H : CONH at position 2); 6.84 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.40 (mt : the 7H corresponding to aromatic H at position 6α and to H at position β of pyridine); 7.45 (broad d, J = 8.5 Hz, 1H : 1' H_4); 7.48 (dd, J = 8.5 and 4 Hz, 1H : 1' H_5); 7.93 (broad d, J = 4 Hz, 1H : 1' H_6); 8.18 (s, 1H : CH=N); 8.36 (d, J = 10 Hz, 1H : CONH at position 1); 8.52 (d, J = 6 Hz, 2H : H at position α of pyridine); 8.72 (d, J = 8 Hz, 1H : CONH at position 6); 11.63 (s, 1H : OH).

Example 52

25 cm^3 of water, 1.1 g of sodium metaperiodate and then 21 mg of ruthenium trichloride are introduced into a three-necked flask Hzcontaining 100 cm^3 of acetonitrile and 5 g of 2"-methylsulphonylpyrimido[4,5-5γ,5δ]pristinamycin I_E and the mixture is kept stirring for 12 hours. An additional 0.55 g of sodium periodate is again added and the mixture is kept stirring for 4 hours. 25 cm^3 of water, 1.25 g of sodium thiosulphate and then 250 cm^3 of methylene chloride and 150 cm^3 of water are added to the reaction mixture. The organic phase is decanted off, dried over magnesium sulphate, filtered and concentrated to dryness at 40°C under reduced pressure (2.7 kPa). The solid obtained is disintegrated in diethyl ether to give 3.57 g of a solid which is purified by 2 flash chromatographies on 250 g and 70 g of silica respectively (eluent: methylene chloride-methanol 95/5 and then 97/3 by volume). The fractions are pooled, dried over magnesium sulphate, filtered and concentrated at 45°C under reduced pressure (2.7 kPa) to give after drying at 40°C (90 Pa) 0.60 g of 2"-methylsulphonylpyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E.

^1H NMR spectrum (400 MHz, $CDCl_3$) : 0.91 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.20 to 1.40 (mt, 3H : 1H of CH_2 at position 3β - 1H of CH_2 at position 3γ and 1H of CH_2 at position 5β); 1.31 (d, J =

7 Hz, 3H : CH_3 at position 1γ); from 1.50 to 1.70 (mt : the 2H corresponding to 1H of CH_2 at position 2β and the other H of CH_2 at position 3γ); 1.74 (mt, 1H : the other H of CH_2 at position 2β); 2.07 (mt, 1H : the other H of CH_2 at position 3β); 2.82 (s, 3H : $ArNCH_3$); 2.88 (dd, J = 12 and 4 Hz, 1H : 1H of CH_2 at position 4β); 3.10 (d, J = 18 Hz, 1H : the other H of CH_2 at position 5β); 3.16 (t, J = 12 Hz, 1H : the other H of CH_2 at position Hz4β); from 3.20 to 3.30 (mt, 1H : 1H of CH_2 at position 3δ); 3.25 (s, 3H : NCH_3); 3.33 (s, 3H : SO_2CH_3); 3.50 (mt, 1H : the other H of CH_2 at position 3γ); 3.82 (d, J = 17.5 Hz, 1H : 1H of CH_2 at position 5ε); 4.12 (unresolved complex, 1H : ARNH); 4.60 (dd, J = 8 and 5.5 Hz, 1H : CH at position 3α); 4.80 (mt, 1H : CH at position 2α); 4.90 (dd, J = 10 and 1 Hz, 1H : CH at position 1α); 4.97 (dd, J = 12 and 4 Hz, 1H : CH at position Hz4α); 5.41 (broad d, J = 6.5 Hz, 1H : CH at position 5α); 5.55 (d, J = 17.5 Hz, 1H : the other H of CH_2 at position Hz5ε); 5.65 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.87 (split q, J = 7 and 1 Hz, 1H : CH at position 1β); 6.05 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.53 (d, J = 10 Hz, 1H : CONH at position 2); 6.72 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.15 to 7.40 (mt : the 5H corresponding to the aromatic H at position 6α); 7.49 (dd, J = 8.5 and 1.5 Hz, 1H : 1' H_4); 7.56 (dd, J = 8.5 and 4 Hz, 1H : 1' H_5); 8.00 (dd, J = 4 and 1.5 Hz, 1H : 1' H_6); 8.38 (d, J = 10 Hz, 1H : CONH at position 1); 8.50 (s, 1H : CH=N);

8.73 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.63 (s, 1H : OH).

2"-methylsulphonylpyrimido[4,5-5γ,5δ]-pristinamycin I_E may be obtained as described in Example 24.

Example 53

0.146 ml of 2-diethylaminoethanethiol and 47 mg of sodium hydride are added to a three-necked flask Hzcontaining 10 cm^3 of dimethylformamide followed, dropwise, by 1 g of potassium salt of 2"-methyl-sulphonylpyrimido[4,5-5γ,5δ]pristinamycin I_E in 10 cm^3 of dimethylformamide. The mixture is kept stirring for one hour at 20°C. The reaction mixture is poured over 100 cm^3 of water and 10 cm^3 of 0.1 N hydrochloric acid are added to pH 7 and then 40 cm^3 of methylene chloride. The aqueous phase is decanted off and extracted with 4 times 40 cm^3 of methylene chloride. The organic phases are combined, dried over magnesium sulphate, filtered and then concentrated under reduced pressure. The solid obtained is disintegrated in ether to give, after filtration, 0.64 g of a solid which is purified by flash chromatography (eluent: methylene chloride-methanol 97/3 by volume). The fractions are pooled, dried over magnesium sulphate, filtered and concentrated at 45°C under reduced pressure (2.7 kPa) to give after drying at 40°C (90 Pa) 0.23 g of 2"-diethylaminoethylthiopyrimido[4,5-5γ,5δ]-pristinamycin I_E.

^{1}H NMR spectrum (400 MHz, $CDCl_3$) : 0.90 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); 1.06 (unresolved complex, 6H : the 2 CH_3 of diethylamine); from 1.20 to 1.35 (mt, 3H : 1H of CH_2 at position 3β - 1H of CH_2 at position 3γ and 1H of CH_2 at position 5β); 1.30 (d, J = 7 Hz, 3H : CH_3 at position 1γ); from 1.50 to 1.65 (mt : the 1H corresponding to the other H of CH_2 at position 3γ); 1.65 and 1.74 (2 mts, 1H each : CH_2 at position 2β); 2.05 (mt, 1H : the other H of CH_2 at position 3β); 2.58 (unresolved complex, 4H : the 2 NCH_2 of diethylamine); 2.79 (mt, 2H : NCH_2); from 2.85 to 3.00 (mt, 2H : 1H of CH_2 at position 4β and the other H of CH_2 at position 5β); 2.88 (s, 6H : $ArN(CH_3)_2$); from 3.10 to 3.30 (mt, 4H : the other H of CH_2 at position 4β - 1H of CH_2 at position 3δ and $ArSCH_2$); 3.26 (s, 3H : NCH_3); 3.50 (mt, 1H : the other H of CH_2 at position 3δ); 3.76 (d, J = 17.5 Hz, 1H : 1H of CH_2 at position 5ε); 4.60 (dd, J = 7.5 and 5.5 Hz, 1H : CH at position 3α); 4.80 (mt, 1H : CH at position 2α); 4.89 (dd, J = 10 and 1 Hz, 1H : CH at position 1α); 5.07 (dd, J = 12 and 4.5 Hz, 1H : CH at position 4α); 5.33 (broad d, J = 5.5 Hz, 1H : CH at position Hz5α); 5.38 (d, J = 17.5 Hz, 1H : the other H of CH_2 at position 5ε); 5.65 (d, J = 8 Hz, 1H : CH at position 6α); 5.88 (split q, J = 7 and 1 Hz, 1H : CH at position Hz1β); 6.34 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.53 (d, J = 10 Hz, 1H : CONH at position 2); 6.85 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.40 (mt :

the 5H corresponding to the aromatic H at position 6α); 7.46 (dd, J = 8.5 and 1.5 Hz, 1H : 1' H_4); 7.49 (dd, J = 8.5 and 4 Hz, 1H : 1' H_5); 7.92 (dd, J = 4 and 1.5 Hz, 1H : 1' H_6); 8.15 (s, 1H : CH=N); 8.38 (d, J = 10 Hz, 1H : CONH at position 1); 8.68 (d, J = 8 Hz, 1H : CONH at position 6); 11.64 (unresolved complex, 1H : OH).

The potassium salt of 2"-methylsulphonyl-pyrimido[4,5-5γ,5δ]pristinamycin I_E may be prepared in the following manner:

1.4 g of potassium bicarbonate are added to a round-bottomed flask placed under argon containing 150 cm^3 of acetone and 10 g of 2"-methylsulphonyl-pyrimido[4,5-5γ,5δ]pristinamycin I_E and the mixture is kept stirring overnight. The cream-coloured precipitate is filtered, washed several times with acetone and with diethyl ether and then filtered, dried under reduced pressure to give 7.4 g of potassium salt of 2"-methylsulphonylpyrimido[4,5-5γ,5δ]pristinamycin I_E which is used as it is.

The 2"-methylsulphonylpyrimido[4,5-5γ,5δ]-pristinamycin I_E may be obtained as described in Example 24.

Example 54

3.7 g of potassium salt of 2"-methyl-sulphonylpyrimido[4,5-5γ,5δ]pristinamycin I_E and 2.2 cm^3 of an 8 M solution of methylamine in ethanol are added to an autoclave containing 37 cm^3 of dimethylformamide and the mixture is heated for 8 hours at 80°C. The

reaction mixture is concentrated to dryness at 50°C under reduced pressure (2.7 kPa) to give 4.1 g of an orange-coloured residue which is taken up in 20 cm^3 of water and 15 cm^3 of ethyl acetate. The organic phase is decanted off, washed with twice 10 cm^3 of water, dried over magnesium sulphate, filtered and concentrated to dryness at 35°C under reduced pressure (2.7 kPa). 0.4 g of a beige solid is thus obtained which is purified by flash chromatography on 40 g of silica (eluent: methylene chloride-methanol 96/4 by volume). The fractions are combined, dried over magnesium sulphate, filtered and concentrated at 45°C under reduced pressure (2.7 kPa) to give 0.16 g of a solid which is crystallized from 3.2 cm^3 of an acetonitrile-water mixture (50/50 by volume). After filtration and then drying at 40°C (90 Pa), 0.13 g of 2"-methylamino-pyrimido[4,5-5γ,5δ]pristinamycin I_E is obtained in the form of beige crystals melting at 210-220°C.

^1H NMR spectrum (400 MHz, $CDCl_3$) : 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.35 (mt, 3H: 1H of CH_2 at position 3β - 1H of CH_2 at position 3γ and 1H of CH_2 at position 5β); 1.30 (d, J = 7 Hz, 3H : CH_3 at position 1γ); from 1.50 to 1.70 (mt : the 2H corresponding to the other H of CH_2 at position 3γ and to 1H of CH_2 at position 2β); 1.74 (mt, 1H : the other H of CH_2 at position 2β); 2.04 (mt, 1H : the other H of CH_2 at position 3β); from 2.80 to 3.00 (mt, 2H : 1H of CH_2 at position 4β and the other H of CH_2 at position

5β); 2.88 (s, 6H : $ArN(CH_3)_2$); 2.97 (d, J = 5 Hz, 3H : $ArNCH_3$); from 3.15 to 3.30 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.25 (s, 3H : NCH_3); 3.48 (mt, 1H : the other H of CH_2 at position 3δ); 3.72 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.60 (dd, J = 8 and 7 Hz, 1H : CH at position 3α); 4.80 (mt, 1H : CH at position 2α); from 4.85 to 4.95 (mt, 2H : CH at position 1α and ArNH); 5.10 (dd, J = 10.5 and 4 Hz, 1H : CH at position 4α); 5.30 (mt, 1H : CH at position 5α); 5.31 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.64 (d, J = 8 Hz, 1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position Hz1β); 6.40 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.54 (d, J = 10 Hz, 1H : CONH at position 2); 6.87 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.15 to 7.40 (mt : the 5H corresponding to the aromatic H at position 6α); 7.44 (limiting AB, 2H : 1' H_4 and 1' H_5); 7.91 (broad d, J = 4 Hz, 1H : 1' H_6); 7.97 (s, 1H : CH=N); 8.38 (d, J = 10 Hz, 1H : CONH at position 1); 8.64 (d, J = 8 Hz, 1H : CONH at position 6); 11.65 (s, 1H : OH).

The potassium salt of 2"-methylsulphonyl-pyrimido[4,5-5γ,5δ]pristinamycin I_E may be prepared according to Example 53.

Example 55

By carrying out the procedure by analogy with Example 32 but starting with 20 cm^3 of methylene chloride, 2.3 g of 2"-(2-pyridyl)pyrimido[4,5-

5γ,5δ]pristinamycin I_E, 0.2 g of ethylene glycol, 2.35 g of acetic acid, 0.48 g of tetra-n-butylammonium periodate and stirring for 12 hours, 3.4 g of a crude product are obtained, which product is dissolved in 70 cm^3 of 0.5 N sulphuric acid. The mixture is extracted with 3 times 50 cm^3 of ethyl acetate. After treatment and concentration, 1.58 g of yellow solid are obtained, which solid is purified by two successive chromatographies, on 100 g and 30 g of silica respectively (eluent: methylene chloride-methanol 95/5 and then methylene chloride-acetonitrile-methanol: 86/8/6 by volume). The fractions are pooled, dried over magnesium sulphate, filtered and then concentrated at 45°C under reduced pressure (2.7 kPa). The solid obtained is taken up in 10 cm^3 of diisopropyl ether, filtered, washed with 10 cm^3 of diisopropyl ether and then dried at 40°C under reduced pressure (90 Pa) to give 0.52 g of 2"-(2-pyridyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E in the form of a pale-yellow solid melting at 209°C.

^1H NMR spectrum (400 MHz, $CDCl_3$) : 0.93 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.25 to 1.40 (mt, 2H: 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.32 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.52 (dd, J = 18 and 6, 1H : 1H of CH_2 at position 5β); 1.62 (mt, 1H : the other H of CH_2 at position 3γ); from 1.60 to 1.85 (mt : the 2H corresponding to CH_2 at position 2β); 2.08 (mt, 1H : the other H of CH_2 at

position 3β); 2.58 (s, 3H : $ArNCH_3$); 2.92 (dd, J = 12 and 4.5 Hz, 1H : 1H of CH_2 at position 4β); from 3.15 to 3.30 (mt, 3H : the other H of CH_2 at position 5β - 1H of CH_2 at position 3δ and the other H of CH_2 at position 4β); 3.27 (s, 3H : NCH_3); 3.51 (mt, 1H : the other H of CH_2 at position 3δ); 3.89 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.63 (dd, J = 8 and 6 Hz, 1H : CH at position 3α); 4.82 (mt, 1H : CH at position 2α); 4.90 (dd, J = 10 and 1 Hz, 1H : CH at position 1α); 5.10 (dd, J = 11 and 4.5 Hz, 1H : CH at position 4α); 5.42 (broad d, J = 6 Hz, 1H : CH at position Hz5α); 5.53 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.69 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.89 (split q, J = 7 and 1 Hz, 1H : CH at position Hz1β); 6.16 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.56 (d, J = 10 Hz, 1H : CONH at position 2); 6.79 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.40 (mt : the 5H corresponding to the aromatic H at position 6α); 7.40 (broad dd, J = 8 and 5 Hz, 1H : H at position 5 of pyridine); 7.48 (dd, J = 8.5 and 1 Hz, 1H : 1' H_4); 7.53 (dd, J = 8.5 and 4 Hz, 1H : 1' H_5); 7.85 (split t, J = 8 and 2 Hz, 1H : H at position 4 of pyridine); 8.01 (dd, J = 4 and 1 Hz, 1H : 1' H_6); 8.43 (d, J = 10 Hz, 1H : CONH at position 1); 8.46 (broad d, J = 8 Hz, H at position 3 of pyridine); 8.56 (s, 1H : CH=N); 8.71 (d, J = 8.5 Hz, 1H : CONH at position 6); 8.84 (broad d, J = 5 Hz, 1H : H at position 6 of pyridine); 11.64 (s, 1H : OH).

2"-(2-pyridyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E may be obtained as described in Example 28.

Example 56

3.9 g of 2"-azidopyrimido[4,5-5γ,5δ]-pristinamycin I_E and 2.16 g of triphenylphosphine are added to a three-necked flask containing 70 cm^3 of tetrahydrofuran and 100 cm^3 of 0.1 N hydrochloric acid and the mixture is kept stirring overnight. The reaction mixture is concentrated to dryness at 40°C under reduced pressure (2.7 kPa); the gummy residue is taken up in 50 cm^3 of water and 100 cm^3 of 0.1 N hydrochloric acid and extracted with 3 times 80 cm^3 of methylene chloride. After decantation, the aqueous phase is neutralized by addition of water saturated with sodium bicarbonate and extracted with 3 times 100 cm^3 of methylene chloride. The organic phases are pooled, dried over magnesium sulphate, filtered and concentrated at 45°C under reduced pressure to give 3.5 g of a yellow solid which is purified by chromatography on 300 g of silica (eluent: methylene chloride-methanol : 96/4 by volume). The fractions are pooled, dried over magnesium sulphate, filtered and concentrated at 45°C under reduced pressure (2.7 kPa) to give a yellow solid which is recrystallized from 40 cm^3 of isopropanol. After filtration, washing with 10 cm^3 of isopropanol and drying at 40°C under reduced pressure, 0.97 g of 2"-aminopyrimido[4,5-5γ,5δ]-

pristinamycin I_E is obtained in the form of a pale-yellow powder melting at 214°C.

2"-azidopyrimido[4,5-5γ,5δ]pristinamycin I_E may be prepared as in Example 25 but starting with 250 cm^3 of dimethylformamide, 10 g of 2"-(4-methylbenzenesulphonyl)pyrimido[4,5-5γ,5δ]pristinamycin I_E, 2.42 g of sodium azide and heating at 65°C for three days. After concentrating the reaction mixture to dryness, 400 cm^3 of water saturated with sodium chloride are added. The orange-yellow precipitate which appeared is filtered and then taken up in 200 cm^3 of methylene chloride. After decantation, drying over magnesium sulphate, filtration and concentration to dryness at 40°C under reduced pressure (2.7 kPa), a solid is obtained which is purified by chromatography on 150 g of silica (eluent: methylene chloride-methanol 96/4 by volume) to give after concentrating the fractions 3.9 g of 2"-azidopyrimido[4,5-5γ,5δ]pristinamycin I_E in the form of an orange-coloured solid which is used as it is.

^1H NMR spectrum (400 MHz, $CDCl_3$) : 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.35 (mt, 3H: 1H of CH_2 at position 3β - 1H of CH_2 at position 3γ and 1H of CH_2 at position 5β); 1.30 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.56 (mt, 1H : the other H of CH_2 at position 3γ); from 1.60 to 1.80 (mt : the 2H corresponding to CH_2 at position 2β); 2.04 (mt, 1H : the other H of CH_2 at position 3β); 2.81 (d, J = 17.5 Hz, 1H

: the other H of CH_2 at position 5β); from 2.85 to 2.95 (mt, 1H : 1H of CH_2 at position 4β); 2.89 (s, 6H : $ArN(CH_3)_2$; from 3.15 to 3.30 (mt, 2H : the other H of CH_2 at position 4β and 1H of CH_2 at position 3δ); 3.25 (s, 3H : NCH_3); 3.49 (mt, 1H : the other H of CH_2 at position 3δ); 3.71 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.60 (dd, J = 8 and 6 Hz, 1H : CH at position 3α); 4.80 (mt, 1H : CH at position 2α); 4.86 (s, 2H : $ArNH_2$); 4.88 (broad d, J = 10 Hz, 1H : CH at position 1α); 5.08 (dd, J = 11.5 and 5 Hz, 1H : CH at position 4α); 5.31 (mt, 1H : CH at position 5α); 5.33 (d, J = 17 Hz, 1H : the other H of CH_2 at position 5ε); 5.64 (d, J = 8.5 Hz, 1H : CH at position 6α); 5.88 (broad q, J = 7 Hz, 1H : CH at position 1β); 6.40 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.54 (d, J = 10 Hz, 1H : CONH at position 2); 6.86 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.20 to 7.35 (mt : the 5H corresponding to the aromatic H at position 6α); 7.42 (dd, J = 8 and 1.5 Hz, 1H : 1' H_4); 7.45 (dd, J = 8 and 4 Hz, 1H : 1' H_5); 7.89 (dd, J = 4 and 1.5 Hz, 1H : 1' H_6); 7.97 (s, 1H : CH=N); 8.36 (d, J = 10 Hz, 1H : CONH at position 1); Hz8.64 (d, J = 8.5 Hz, 1H : CONH at position 6); 11.65 (s, 1H : OH).

2"-(4-methylbenzenesulphonyl)pyrimido[4,5-5γ,5δ]pristinamycin I_E may be obtained as described in Example 25.

Example 57

1 g of 2"-hydroxymethylpyrido[2,3-5γ,5δ]-

pristinamycin I_E and 0.155 cm^3 of thionyl chloride are added to a three-necked flask placed under a nitrogen stream and containing 10 cm^3 of acetonitrile. The mixture is kept stirring for 30 minutes and 0.9 cm^3 of triethylamine is added. After filtering the triethylamine hydrochloride formed, a solution of the sodium salt of 2-diethylaminoethanethiol (obtained after stirring for 30 minutes from 0.324 cm^3 of diethylaminoethanethiol and 102 mg of sodium hydride in 20 cm^3 of acetonitrile) are added. After heating at 50°C for 3 hours, the insoluble matter is removed by filtration and then washed with 20 cm^3 of acetonitrile. The filtrate is concentrated to dryness under reduced pressure (45°C - 2.7 kPa) and then the residue is taken up in 50 cm^3 of methylene chloride and 50 cm^3 of water. The organic phase is decanted off, washed with 25 cm^3 of water, dried over sodium sulphate and then filtered to give, after concentration to dryness, 1.1 g of a residue which is chromatographed on 50 g of silica (eluent: methylene chloride-methanol Hzgradient 98/2 to 90/10 by volume) to give 150 mg of product which is purified by HPLC on 450 g of 10 µm C_8 silica (eluent: water-acetonitrile 70/30 by volume, containing 0.1% trifluoroacetic acid). The fractions are combined and then the acetonitrile removed at 40°C under reduced pressure (2.7 kPa). The aqueous phase is adjusted to pH 7-8 by addition of water saturated with sodium bicarbonate and then extracted with twice 25 cm^3 of

methylene chloride. The organic phase is dried over sodium sulphate, filtered and then concentrated to dryness to give 30 mg of 2"-diethylaminoethylthio-methylpyrido[2,3-5γ,5δ]pristinamycin I_E in the form of a yellow solid melting at 132°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$) : 0.92 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); 1.02 (t, J = 7 Hz, 6H : CH_3 of diethylamino); from 1.20 to 1.35 (mt, 2H: 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.29 (d, J = 7 Hz, 3H : CH_3 at position 1γ); 1.57 (mt, 1H : the other H of CH_2 at position 3γ); from 1.60 to 1.80 (mt : the 2H corresponding to the CH_2 at position 2β); 1.88 (very broad d, J = 16.5 Hz, 1H : 1H of CH_2 at position 5β); 2.03 (mt, 1H : the other H of CH_2 at position 3β); from 2.45 to 2.65 (unresolved complex, 4H : NCH_2 of diethylamino); from 2.60 to 2.75 (mt, 4H : SCH_2CH_2N); 2.84 (s, 6H : $ArN(CH_3)_2$); 2.98 (dd, J = 13.5 and 6 Hz, 1H : 1H of CH_2 at position 4β); from 3.10 to 3.30 (mt, 3H : the other H of CH_2 at position 4β - the other H of CH_2 at position 5β and 1H of CH_2 at position 3δ); 3.20 (s, 3H : NCH_3); 3.49 (mt, 1H : the other H of CH_2 at position 3δ); 3.79 (s, 2H : $ArCH_2S$); 3.94 (d, J = 17 Hz, 1H : 1H of CH_2 at position 5ε); 4.60 (dd, J = 8 and 5.5 Hz, 1H : CH at position 3α); 4.79 (mt, 1H : CH at position 2α); 4.87 (dd, J = 10 and 1 Hz, 1H : CH at position 1α); 5.28 (dd, J = 9 and 6 Hz, 1H : CH at position 4α); 5.44 (broad d, J = 5.5 Hz, 1H : CH at position 5α); 5.44 (d, J = 17 Hz, 1H : the other H of

CH_2 at position 5ε); 5.60 (d, J = 8 Hz, 1H : CH at position 6α); 5.87 (split q, J = 7 and 1 Hz, 1H : CH at position 1β); 6.36 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.57 (d, J = 10 Hz, 1H : CONH at position 2); 6.84 (d, J = 8 Hz, 2H : aromatic H at position 4δ); 7.20 (d, J = 8 Hz, 1H : aromatic H at position β with respect to N); from 7.20 to 7.40 (mt : the 8H corresponding to the 5 aromatic H at position 6α - to the aromatic H at position γ with respect to N - to 1' H_4 and to 1' H_5); 7.83 (dd, J = 4 and 1 Hz, 1H : 1' H_6); 8.40 (d, J = 10 Hz, 1H : CONH at position 1); 8.67 (d, J = 8 Hz, 1H : CONH at position 6); 11.65 (broad unresolved complex, 1H : OH).

2"-hydroxymethylpyrido[2,3-5γ,5β]-pristinamycin I_E may be obtained as described in Example 11.

Example 58

· 4ε-Chloro-2"-tert-butylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 2"-tert-Butylpyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-tert-butylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-aminopyrido[2,3-5γ,5δ]pristinamycin I_E

· 2"-Aminopyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-aminopyrido[2,3-5γ,5δ](4ζ-methyl-amino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-3"-methoxycarbonyl-2"-methylpyrido[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Chloro-2"-phenylpyrido[2,3-5γ,5δ]pristinamycin I_E

· 2"-Phenylpyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-phenylpyrido[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-(4-aminophenyl)pyrido-[2,3-5γ,5δ]pristinamycin I_E

· 2"-(4-Aminophenyl)pyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-(4-aminophenyl)pyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-(4-diethylaminophenyl)pyrido[2,3-5γ,5δ]pristinamycin I_E

· 2"-(4-Diethylaminophenyl)pyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-(4-diethylaminophenyl)pyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloropyrido[2,3-5γ,5δ]pristinamycin I_E

· Pyrido[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloropyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-chloromethylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 2"-Chloromethylpyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-chloromethylpyrido[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-3"-methoxycarbonyl-2"-methylpyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-Chloro-2"-(2-pyridyl)pyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Chloro-2"-morpholinomethylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 2"-Morpholinomethylpyrido[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-morpholinomethylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-(3-pyridyl)pyrido[2,3-5γ,5δ]-pristinamycin I_E

· 2"-(3-Pyridyl)pyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-(3-pyridyl)pyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-(4-methyl-1-piperazinylmethyl)pyrido-[2,3-5γ,5δ]pristinamycin I_E

· 2"-(4-Methyl-1-piperazinylmethyl)pyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-Chloro-2"-(4-methyl-1-piperazinylmethyl)pyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-

pristinamycin I_E

· 4ε-Chloro-2"-methylpyrido[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-cyclopropylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 2"-Cyclopropylpyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-cyclopropylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-hydroxymethylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 2"-Hydroxymethylpyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-hydroxymethylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-propylpyrido[2,3-5γ,5δ]pristinamycin I_E

· 2"-Propylpyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-propylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-isopropylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 2"-Isopropylpyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-isopropylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-acetoxymethylpyrido[2,3-5γ,5δ]-

pristinamycin I_E

· 2"-Acetoxymethylpyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-acetoxymethylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-cyclopropylaminomethylpyrido-[2,3-5γ,5δ]pristinamycin I_E

· 2"-Cyclopropylaminomethylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2",3"-dimethylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-ethoxycarbonylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 2"-Ethoxycarbonylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-ethoxycarbonylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· PIA Cl: 4ε-chloro-2"-(N-diethylaminomethyl)pyrido-[2,3-5γ,5δ]pristinamycin I_E

· PIB: 2"-(N-diethylaminomethyl)pyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· PIB Cl: 4ε-chloro-2"-(N-diethylaminomethyl)pyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· PIA Cl: 4ε-chloro-2"-carbamoylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· PIB: 2"-carbamoylpyrido[2,3-5γ,5δ](4ζ-methyl-amino)(4ζ-dedimethylamino)pristinamycin I_E

· PIB Cl: 4ε-chloro-2"-carbamoylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· PIA Cl: 4ε-chloro-2"-diethylaminoethylthiomethyl-pyrido[2,3-5γ,5δ]pristinamycin I_E

· PIB: 2"-diethylaminoethylthiomethylpyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· PIB Cl: 4ε-chloro-2"-diethylaminoethylthiomethyl-pyrido[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· PIA Cl: 4ε-chloro-2"-(morpholinoethylthiomethyl)-pyrido[2,3-5γ,5δ]pristinamycin I_E

· PIB: 2"-(morpholinoethylthiomethyl)pyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-Chloro-2"-(morpholinoethylthiomethyl)pyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-Chloro-2"-(1-pyrrolidinoethylthiomethyl)pyrido-[2,3-5γ,5δ]pristinamycin I_E

· 2"-(1-Pyrrolidinoethylthiomethyl)pyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-Chloro-2"-(1-pyrrolidinoethylthiomethyl)pyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-Chloro-2"-(piperidinoethylthiomethyl)pyrido-[2,3-5γ,5δ]pristinamycin I_E

· 2"-(Piperidinoethylthiomethyl)pyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Chloro-2"-(piperidinoethylthiomethyl)pyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-Bromo-2"-tert-butylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-tert-butylpyrido[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-tert-butylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-tert-butylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-tert-butylpyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-tert-butylpyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-tert-Butylpyrido[2,3-5γ,5δ](4ζ-diethylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-tert-Butylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-tert-Butylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-tert-Butylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-tert-Butylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-

pristinamycin I_E

· 2"-tert-Butylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-tert-Butylpyrido[2,3-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-tert-Butylpyrido[2,3-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-aminopyrido[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Bromo-2"-aminopyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-aminopyrido[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Allyl-2"-aminopyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)2"-aminopyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)2"-aminopyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Aminopyrido[2,3-5γ,5δ](4ζ-diethylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Aminopyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Aminopyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Aminopyrido[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Aminopyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-

pristinamycin I_E

· 2"-Aminopyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Aminopyrido[2,3-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Aminopyrido[2,3-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-3"-methoxycarbonyl-2"-methylpyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Bromo-3"-methoxycarbonyl-2"-methylpyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-Allyl-3"-methoxycarbonyl-2"-methylpyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Allyl-3"-methoxycarbonyl-2"-methylpyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-3"-methoxycarbonyl-2"-methylpyrido[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-3"-methoxycarbonyl-2"-methylpyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 3"-Methoxycarbonyl-2"-methylpyrido[2,3-5γ,5δ]-(4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 3"-Methoxycarbonyl-2"-methylpyrido[2,3-5γ,5δ]-(4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 3"-Methoxycarbonyl-2"-methylpyrido[2,3-5γ,5δ]-(4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 3"-Methoxycarbonyl-2"-methylpyrido[2,3-5γ,5δ]-(4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 3"-Methoxycarbonyl-2"-methylpyrido[2,3-5γ,5δ]-(4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethyl-amino)pristinamycin I_E

· 3"-Methoxycarbonyl-2"-methylpyrido[2,3-5γ,5δ]-(4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethyl-amino)pristinamycin I_E

· 3"-Methoxycarbonyl-2"-methylpyrido[2,3-5γ,5δ]-(4ζ-methyl)(4ζ-dedimethylamino)pristinamycin I_E

· 3"-Methoxycarbonyl-2"-methylpyrido[2,3-5γ,5δ]-(4ζ-tert-butyl)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-phenylpyrido[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Bromo-2"-phenylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-phenylpyrido[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Allyl-2"-phenylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-phenylpyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-phenylpyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Phenylpyrido[2,3-5γ,5δ](4ζ-diethylamino)-

(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Phenylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Phenylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Phenylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Phenylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Phenylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Phenylpyrido[2,3-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Phenylpyrido[2,3-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-(4-aminophenyl)pyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-(4-aminophenyl)pyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-(4-aminophenyl)pyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-(4-aminophenyl)pyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(4-aminophenyl)-pyrido[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(4-aminophenyl)-pyrido[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(4-Aminophenyl)pyrido[2,3-5γ,5δ]-(4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Aminophenyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Aminophenyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Aminophenyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Aminophenyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(4-Aminophenyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(4-Aminophenyl)pyrido[2,3-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Aminophenyl)pyrido[2,3-5γ,5δ](4ζ-tert-butyl)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-(4-diethylaminophenyl)pyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Bromo-2"-(4-diethylaminophenyl)pyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-Allyl-2"-(4-diethylaminophenyl)pyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Allyl-2"-(4-diethylaminophenyl)pyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(4-diethylamino-phenyl)pyrido[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(4-diethylamino-phenyl)pyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Diethylaminophenyl)pyrido[2,3-5γ,5δ]-(4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Diethylaminophenyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Diethylaminophenyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Diethylaminophenyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Diethylaminophenyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(4-Diethylaminophenyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(4-Diethylaminophenyl)pyrido[2,3-5γ,5δ]-(4ζ-methyl)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Diethylaminophenyl)pyrido[2,3-5γ,5δ]-(4ζ-tert-butyl)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromopyrido[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Bromopyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allylpyrido[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Allylpyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)pyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)pyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· Pyrido[2,3-5γ,5δ](4ζ-diethylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· Pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· Pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· Pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· Pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)-amino)(4ζ-dedimethylamino)pristinamycin I_E

· Pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)-amino)(4ζ-dedimethylamino)pristinamycin I_E

· Pyrido[2,3-5γ,5δ](4ζ-methyl)(4ζ-dedimethylamino)-pristinamycin I_E

· Pyrido[2,3-5γ,5δ](4ζ-tert-butyl)(4ζ-dedimethyl-amino)pristinamycin I_E

· 4ε-Bromo-2"-chloromethylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-chloromethylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-chloromethylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-chloromethylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-chloromethylpyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-chloromethylpyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Chloromethylpyrido[2,3-5γ,5δ](4ζ-diethylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Chloromethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Chloromethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Chloromethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Chloromethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Chloromethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Chloromethylpyrido[2,3-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Chloromethylpyrido[2,3-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-(2-pyridyl)pyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-(2-pyridyl)pyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-(2-pyridyl)pyrido[2,3-5γ,5δ]-

pristinamycin I_E

· 4ε-Allyl-2"-(2-pyridyl)pyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(2-pyridyl)pyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(2-pyridyl)pyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(2-Pyridyl)pyrido[2,3-5γ,5δ](4ζ-diethylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Pyridyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Pyridyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Pyridyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Pyridyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(2-Pyridyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(2-Pyridyl)pyrido[2,3-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Pyridyl)pyrido[2,3-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-morpholinomethylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-morpholinomethylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-morpholinomethylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-morpholinomethylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-morpholinomethyl-pyrido[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-morpholinomethyl-pyrido[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Morpholinomethylpyrido[2,3-5γ,5δ]-(4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Morpholinomethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Morpholinomethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Morpholinomethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Morpholinomethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Morpholinomethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Morpholinomethylpyrido[2,3-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Morpholinomethylpyrido[2,3-5γ,5δ](4ζ-tert-

butyl)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-(3-pyridyl)pyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-(3-pyridyl)pyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-(3-pyridyl)pyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-(3-pyridyl)pyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(3-pyridyl)pyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(3-pyridyl)pyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(3-Pyridyl)pyrido[2,3-5γ,5δ](4ζ-diethylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(3-Pyridyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(3-Pyridyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(3-Pyridyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(3-Pyridyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(3-Pyridyl)pyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(3-Pyridyl)pyrido[2,3-5γ,5δ](4-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(3-Pyridyl)pyrido[2,3-5γ,5δ](4-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-(4-methyl-1-piperazinylmethyl)pyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Bromo-2"-(4-methyl-1-piperazinylmethyl)pyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-Allyl-2"-(4-methyl-1-piperazinylmethyl)pyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Allyl-2"-(4-methyl-1-piperazinylmethyl)pyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(4-methyl-1-piperazinylmethyl)pyrido[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(4-methyl-1-piperazinylmethyl)pyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Methyl-1-piperazinylmethyl)pyrido-[2,3-5γ,5δ](4ζ-diethylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(4-Methyl-1-piperazinylmethyl)pyrido-[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethyl-amino)pristinamycin I_E

· 2"-(4-Methyl-1-piperazinylmethyl)pyrido-[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethyl-amino)pristinamycin I_E

· 2"-(4-Methyl-1-piperazinylmethyl)pyrido-[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethyl-amino)pristinamycin I_E

· 2"-(4-Methyl-1-piperazinylmethyl)pyrido-[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Methyl-1-piperazinylmethyl)pyrido-[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Methyl-1-piperazinylmethyl)pyrido-[2,3-5γ,5δ](4ζ-methyl)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Methyl-1-piperazinylmethyl)pyrido-[2,3-5γ,5δ](4ζ-tert-butyl)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-Bromo-2"-ethylpyrido[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Bromo-2"-ethylpyrido[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-ethylpyrido[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Allyl-2"-ethylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-ethylpyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-ethylpyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Ethylpyrido[2,3-5γ,5δ](4ζ-diethylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Ethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Ethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Ethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Ethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Ethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Ethylpyrido[2,3-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Ethylpyrido[2,3-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-cyclopropylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-cyclopropylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-cyclopropylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-cyclopropylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-cyclopropylpyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-cyclopropylpyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-

pristinamycin I_E

· 2"-Cyclopropylpyrido[2,3-5γ,5δ](4ζ-diethylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Cyclopropylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Cyclopropylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Cyclopropylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Cyclopropylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Cyclopropylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Cyclopropylpyrido[2,3-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Cyclopropylpyrido[2,3-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-hydroxymethylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-hydroxymethylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-hydroxymethylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-hydroxymethylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-hydroxymethylpyrido-

[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-hydroxymethylpyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Hydroxymethylpyrido[2,3-5γ,5δ](4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Hydroxymethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Hydroxymethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Hydroxymethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Hydroxymethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Hydroxymethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Hydroxymethylpyrido[2,3-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Hydroxymethylpyrido[2,3-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-propylpyrido[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Bromo-2"-propylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-propylpyrido[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Allyl-2"-propylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-propylpyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-propylpyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Propylpyrido[2,3-5γ,5δ](4ζ-diethylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Propylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Propylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Propylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Propylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Propylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Propylpyrido[2,3-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Propylpyrido[2,3-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-isopropylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-isopropylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-isopropylpyrido[2,3-5γ,5δ]-

pristinamycin I_E

· 4ε-Allyl-2"-isopropylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-isopropylpyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-isopropylpyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Isopropylpyrido[2,3-5γ,5δ](4ζ-diethylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Isopropylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Isopropylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Isopropylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Isopropylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Isopropylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Isopropylpyrido[2,3-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Isopropylpyrido[2,3-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-acetoxymethylmethylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-acetoxymethylmethylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-acetoxymethylmethylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-acetoxymethylmethylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-acetoxymethylpyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-acetoxymethylpyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Acetoxymethylpyrido[2,3-5γ,5δ](4ζ-diethyl-amino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Acetoxymethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Acetoxymethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Acetoxymethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Acetoxymethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Acetoxymethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Acetoxymethylpyrido[2,3-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Acetoxymethylpyrido[2,3-5γ,5δ](4ζ-tert-butyl)-

(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-cyclopropylaminomethylpyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Bromo-2"-cyclopropylaminomethylpyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-Allyl-2"-cyclopropylaminomethylpyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Allyl-2"-cyclopropylaminomethylpyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-cyclopropylamino-methylpyrido[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-cyclopropylamino-methylpyrido[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethyl-amino)pristinamycin I_E

· 2"-Cyclopropylaminomethylpyrido[2,3-5γ,5δ](4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Cyclopropylaminomethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Cyclopropylaminomethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Cyclopropylaminomethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Cyclopropylaminomethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Cyclopropylaminomethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Cyclopropylaminomethylpyrido[2,3-5γ,5δ](4ζ-methyl)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Cyclopropylaminomethylpyrido[2,3-5γ,5δ](4ζ-tert-butyl)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2",3"-dimethylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2",3"-dimethylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2",3"-dimethylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2",3"-dimethylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2",3"-dimethylpyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2",3"-dimethylpyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2",3"-Dimethylpyrido[2,3-5γ,5δ](4ζ-diethylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2",3"-Dimethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2",3"-Dimethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2",3"-Dimethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2",3"-Dimethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)pristinamycin I_E

· 2",3"-Dimethylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)pristinamycin I_E

· 2",3"-Dimethylpyrido[2,3-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2",3"-Dimethylpyrido[2,3-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-ethoxycarbonylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-ethoxycarbonylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-ethoxycarbonylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-ethoxycarbonylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-ethoxycarbonylpyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-ethoxycarbonylpyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Ethoxycarbonylpyrido[2,3-5γ,5δ](4ζ-diethyl-amino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Ethoxycarbonylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Ethoxycarbonylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Ethoxycarbonylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-

propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Ethoxycarbonylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Ethoxycarbonylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Ethoxycarbonylpyrido[2,3-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Ethoxycarbonylpyrido[2,3-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-(N-diethylaminomethyl)pyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Bromo-2"-(N-diethylaminomethyl)pyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-Allyl-2"-(N-diethylaminomethyl)pyrido-[2,3-5γ,5δ]pristinamycin I_E

· 4ε-Allyl-2"-(N-diethylaminomethyl)pyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(N-diethylamino-methyl)pyrido[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(N-diethylamino-methyl)pyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(N-Diethylaminomethyl)pyrido[2,3-5γ,5δ]-(4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(N-Diethylaminomethyl)pyrido[2,3-5γ,5δ]-(4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(N-Diethylaminomethyl)pyrido[2,3-5γ,5δ]-(4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(N-Diethylaminomethyl)pyrido[2,3-5γ,5δ]-(4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(N-Diethylaminomethyl)pyrido[2,3-5γ,5δ]-(4ζ-N-methyl-N-(4-pyridylmethyl)amino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(N-Diethylaminomethyl)pyrido[2,3-5γ,5δ]-(4ζ-N-methyl-N-(3-pyridylmethyl)amino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(N-Diethylaminomethyl)pyrido[2,3-5γ,5δ]-(4ζ-methyl)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(N-Diethylaminomethyl)pyrido[2,3-5γ,5δ]-(4ζ-tert-butyl)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-carbamoylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-carbamoylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-carbamoylpyrido[2,3-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-carbamoylpyrido[2,3-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-methylpropen-1-yl)-2"-carbamoylpyrido-

[2,3-5γ,5δ]pristinamycin I_E

· 4ε-(2-methylpropen-1-yl)-2"-carbamoylpyrido-[2,3-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Carbamoylpyrido[2,3-5γ,5δ](4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Carbamoylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Carbamoylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Carbamoylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Carbamoylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Carbamoylpyrido[2,3-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Carbamoylpyrido[2,3-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Carbamoylpyrido[2,3-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methoxypyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methoxypyrimido[4,5-5γ,5δ]-4ε-chloro-pristinamycin I_E

· 2"-Methoxypyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)-4ε-chloropristinamycin I_E

· 2"-(4-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Pyridyl)pyrimido[4,5-5γ,5δ]-4ε-chloro-pristinamycin I_E

· 2"-(4-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-methyl-amino)(4ζ-dedimethylamino)-4ε-chloropristinamycin I_E

· 2"-Methylthiopyrimido[4,5-5γ,5δ]-4ε-chloro-pristinamycin I_E

· 2"-(3-Aminophenyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(3-Aminophenyl)pyrimido[4,5-5γ,5δ]-4ε-chloropristinamycin I_E

· 2"-(3-Aminophenyl)pyrimido[4,5-5γ,5δ](4ζ-methyl-amino)(4ζ-dedimethylamino)-4ε-chloropristinamycin I_E

· 2"-Methylthiopyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)-4ε-chloropristinamycin I_E

· 2"-(1-Pyrrolidinyl)pyrimido[4,5-5γ,5δ]-4ε-chloropristinamycin I_E

· 2"-(1-Azetidinyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(1-Azetidinyl)pyrimido[4,5-5γ,5δ]-4ε-chloropristinamycin I_E

· 2"-(1-Azetidinyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)-4ε-chloro-pristinamycin I_E

· 2"-(3-Pyridyl)pyrimido[4,5-5γ,5δ]pristinamycin I_E

· 2"-(3-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(3-Pyridyl)pyrimido[4,5-5γ,5δ]-4ε-chloro-pristinamycin I_E

· 2"-(3-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-methyl-amino)(4ζ-dedimethylamino)-4ε-chloropristinamycin I_E

· 2"-(2-Pyridyl)pyrimido[4,5-5γ,5δ]-4ε-chloro-pristinamycin I_E

· 2"-(1-Pyrrolidinyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)-4ε-chloro-pristinamycin I_E

· 2"-Methylpyrimido[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methylpyrimido[4,5-5γ,5δ]-4ε-chloro-pristinamycin I_E

· 2"-Methylpyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)-4ε-chloropristinamycin I_E

· 2"-(2-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)-4ε-chloropristinamycin I_E

· 2"-(2-Pyrazinyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Pyrazinyl)pyrimido[4,5-5γ,5δ]-4ε-chloro-pristinamycin I_E

· 2"-(2-Pyrazinyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)-4ε-chloro-pristinamycin I_E

· 2"-(2-Morpholinoethylthio)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Morpholinoethylthio)pyrimido[4,5-5γ,5δ]-4ε-chloropristinamycin I_E

- 2"-(2-Morpholinoethylthio)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)-4ε-chloro-pristinamycin I_E
- 2"-Aminopyrimido[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E
- 2"-Aminopyrimido[4,5-5γ,5δ]-4ε-chloropristinamycin I_E
- 2"-Aminopyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)-4ε-chloropristinamycin I_E
- 2"-(1-Pyrazol)pyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E
- 2"-(1-Pyrazol)pyrimido[4,5-5γ,5δ]-4ε-chloro-pristinamycin I_E
- 2"-(1-Pyrazol)pyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)-4ε-chloropristinamycin I_E
- 2"-(Diethylaminoethylthio)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E
- 2"-(Diethylaminoethylthio)pyrimido[4,5-5γ,5δ]-4ε-chloropristinamycin I_E
- 2"-(Diethylaminoethylthio)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)-4ε-chloropristinamycin I_E
- 2"-Methylaminopyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E
- 2"-Methylaminopyrimido[4,5-5γ,5δ]-4ε-chloro-pristinamycin I_E
- 2"-Methylaminopyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)-4ε-chloropristinamycin I_E

- 2"-Methylsulphonylpyrimido[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E
- 2"-Methylsulphonylpyrimido[4,5-5γ,5δ]-4ε-chloropristinamycin I_E
- 2"-Methylsulphonylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)-4ε-chloropristinamycin I_E
- 2"-(4-Aminophenyl)pyrimido[4,5-5γ,5δ]pristinamycin I_E
- 2"-(4-Aminophenyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E
- 2"-(4-Aminophenyl)pyrimido[4,5-5γ,5δ]-4ε-chloropristinamycin I_E
- 2"-(4-Aminophenyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)-4ε-chloropristinamycin I_E
- 2"-Trifluoromethylpyrimido[4,5-5γ,5δ]pristinamycin I_E
- 2"-Trifluoromethylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E
- 2"-Trifluoromethylpyrimido[4,5-5γ,5δ]-4ε-chloropristinamycin I_E
- 2"-Trifluoromethylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)-4ε-chloropristinamycin I_E
- 2"-Cyclopropylpyrimido[4,5-5γ,5δ]pristinamycin I_E
- 2"-Cyclopropylpyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Cyclopropylpyrimido[4,5-5γ,5δ]-4ε-chloropristinamycin I_E

· 2"-Cyclopropylpyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)-4ε-chloropristinamycin I_E

· 2"-Morpholinomethylpyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 2"-Morpholinomethylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Morpholinomethylpyrimido[4,5-5γ,5δ]-4ε-chloro-pristinamycin I_E

· 2"-Morpholinomethylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)-4ε-chloro-pristinamycin I_E

· 2"-Ethylpyrimido[4,5-5γ,5δ]pristinamycin I_E

· 2"-Ethylpyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Ethylpyrimido[4,5-5γ,5δ]-4ε-chloropristinamycin I_E

· 2"-Ethylpyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)-4ε-chloropristinamycin I_E

· 2"-Propylpyrimido[4,5-5γ,5δ]pristinamycin I_E

· 2"-Propylpyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Propylpyrimido[4,5-5γ,5δ]-4ε-chloro-pristinamycin I_E

· 2"-Propylpyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)-4ε-chloropristinamycin I_E

· 2"-Isopropylpyrimido[4,5-5γ,5δ]pristinamycin I_E

· 2"-Isopropylpyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Isopropylpyrimido[4,5-5γ,5δ]-4ε-chloro-pristinamycin I_E

· 2"-Isopropylpyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)-4ε-chloropristinamycin I_E

· 2"-Cyclopropylaminomethylpyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 2"-Cyclopropylaminomethylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Cyclopropylaminomethylpyrimido[4,5-5γ,5δ]-4ε-chloropristinamycin I_E

· 2"-Cyclopropylaminomethylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)-4ε-chloropristinamycin I_E

· 4ε-Bromo-2"-methoxypyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-methoxypyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-methoxypyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-methoxypyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-methylpropen-1-yl)-2"-methoxypyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-methylpropen-1-yl)-2"-methoxypyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Methoxypyrimido[4,5-5γ,5δ](4ζ-diethylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methoxypyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methoxypyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methoxypyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methoxypyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Methoxypyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Methoxypyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methoxypyrimido[4,5-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-(4-pyridyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-(4-pyridyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-(4-pyridyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-(4-pyridyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(4-pyridyl)pyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(4-pyridyl)pyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(4-Pyridyl)pyrimido[4,5-5γ,5δ]-(4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(4-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(4-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-methylthiopyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-methylthiopyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-methylthiopyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-methylthiopyrimido[4,5-5γ,5δ]-

(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-methylthiopyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-methylthiopyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Methylthiopyrimido[4,5-5γ,5δ](4ζ-diethylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methylthiopyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methylthiopyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methylthiopyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methylthiopyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Methylthiopyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Methylthiopyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methylthiopyrimido[4,5-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-(3-aminophenyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-(3-aminophenyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-(3-aminophenyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-(3-aminophenyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(3-aminophenyl)-pyrimido[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(3-aminophenyl)-pyrimido[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethyl-amino)pristinamycin I_E

· 2"-(3-Aminophenyl)pyrimido[4,5-5γ,5δ]-(4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(3-Aminophenyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(3-Aminophenyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(3-Aminophenyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(3-Aminophenyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(3-Aminophenyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(3-Aminophenyl)pyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(3-Aminophenyl)pyrimido[4,5-5γ,5δ](4ζ-tert-butyl)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-(1-pyrrolidinyl)pyrimido[4,5-5γ,5δ]-

(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-(1-pyrrolidinyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-(1-pyrrolidinyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(1-pyrrolidinyl)-pyrimido[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(1-pyrrolidinyl)-pyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(1-Pyrrolidinyl)pyrimido[4,5-5γ,5δ](4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(1-Pyrrolidinyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(1-Pyrrolidinyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(1-Pyrrolidinyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(1-Pyrrolidinyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(1-Pyrrolidinyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(1-Pyrrolidinyl)pyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(1-Pyrrolidinyl)pyrimido[4,5-5γ,5δ](4ζ-tert-

butyl)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-(1-azetidinyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-(1-azetidinyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-(1-azetidinyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-(1-azetidinyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(1-azetidinyl)-pyrimido[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(1-azetidinyl)-pyrimido[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethyl-amino)pristinamycin I_E

· 2"-(1-Azetidinyl)pyrimido[4,5-5γ,5δ]-(4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(1-Azetidinyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(1-Azetidinyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(1-Azetidinyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(1-Azetidinyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(1-Azetidinyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(1-Azetidinyl)pyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(1-Azetidinyl)pyrimido[4,5-5γ,5δ](4ζ-tert-butyl)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-(3-pyridyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-(3-pyridyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-(3-pyridyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-(3-pyridyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(3-pyridyl)pyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(3-pyridyl)pyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(3-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(3-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(3-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(3-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(3-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(3-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(3-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(3-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-(2-pyridyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-(2-pyridyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-(2-pyridyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-(2-pyridyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(2-pyridyl)pyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(2-pyridyl)pyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(2-Pyridyl)pyrimido[4,5-5γ,5δ]-(4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(2-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(2-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Pyridyl)pyrimido[4,5-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-methylpyrimido[4,5-5γ,5δ]pristinamycin I_E

· 4ε-Bromo-2"-methylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-methylpyrimido[4,5-5γ,5δ]pristinamycin I_E

· 4ε-Allyl-2"-methylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-methylpyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-methylpyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Methylpyrimido[4,5-5γ,5δ](4ζ-diethylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-

ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Methylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Methylpyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methylpyrimido[4,5-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-(2-pyrazinyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-(2-pyrazinyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-(2-pyrazinyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-(2-pyrazinyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-methylpropen-1-yl)-2"-(2-pyrazinyl)pyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-methylpropen-1-yl)-2"-(2-pyrazinyl)pyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(2-Pyrazinyl)pyrimido[4,5-5γ,5δ]-(4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Pyrazinyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Pyrazinyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Pyrazinyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Pyrazinyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(2-Pyrazinyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(2-Pyrazinyl)pyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Pyrazinyl)pyrimido[4,5-5γ,5δ](4ζ-tert-butyl)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-(2-morpholinoethylthio)pyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-Bromo-2"-(2-morpholinoethylthio)pyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-Allyl-2"-(2-morpholinoethylthio)pyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-Allyl-2"-(2-morpholinoethylthio)pyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-(2-methylpropen-1-yl)-2"-(2-morpholino-ethylthio)pyrimido[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-methylpropen-1-yl)-2"-(2-morpholino-ethylthio)pyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Morpholinoethylthio)pyrimido[4,5-5γ,5δ]-(4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Morpholinoethylthio)pyrimido[4,5-5γ,5δ]-(4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(2-Morpholinoethylthio)pyrimido[4,5-5γ,5δ]-(4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(2-Morpholinoethylthio)pyrimido[4,5-5γ,5δ]-(4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(2-Morpholinoethylthio)pyrimido[4,5-5γ,5δ]-(4ζ-N-methyl-N-(4-pyridylmethyl)amino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Morpholinoethylthio)pyrimido[4,5-5γ,5δ]-(4ζ-N-methyl-N-(3-pyridylmethyl)amino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Morpholinoethylthio)pyrimido[4,5-5γ,5δ]-(4ζ-methyl)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(2-Morpholinoethylthio)pyrimido[4,5-5γ,5δ]-(4ζ-tert-butyl)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-aminopyrimido[4,5-5γ,5δ]pristinamycin I_E

· 4ε-Bromo-2"-aminopyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-aminopyrimido[4,5-5γ,5δ]pristinamycin I_E

· 4ε-Allyl-2"-aminopyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-aminopyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-aminopyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Aminopyrimido[4,5-5γ,5δ](4ζ-diethylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Aminopyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Aminopyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Aminopyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Aminopyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Aminopyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Aminopyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Aminopyrimido[4,5-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-(1-pyrazolyl)pyrimido[4,5-5γ,5δ]-

pristinamycin I_E

· 4ε-Bromo-2"-(1-pyrazolyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-(1-pyrazolyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-(1-pyrazolyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(1-pyrazolyl)pyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(1-pyrazolyl)pyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(1-Pyrazolyl)pyrimido[4,5-5γ,5δ](4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(1-Pyrazolyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(1-Pyrazolyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(1-Pyrazolyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(1-Pyrazolyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(1-Pyrazolyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(1-Pyrazolyl)pyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(1-Pyrazolyl)pyrimido[4,5-5γ,5δ](4ζ-tert-butyl)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-(diethylaminoethylthio)pyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-Bromo-2"-(diethylaminoethylthio)pyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-Allyl-2"-(diethylaminoethylthio)pyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-Allyl-2"-(diethylaminoethylthio)pyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(diethylaminoethyl-thio)pyrimido[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(diethylaminoethyl-thio)pyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(1-Pyrazolyl)pyrimido[4,5-5γ,5δ](4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(Diethylaminoethylthio)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(Diethylaminoethylthio)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(Diethylaminoethylthio)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(Diethylaminoethylthio)pyrimido[4,5-5γ,5δ]-(4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(Diethylaminoethylthio)pyrimido[4,5-5γ,5δ]-(4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(Diethylaminoethylthio)pyrimido[4,5-5γ,5δ]-(4ζ-methyl)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(Diethylaminoethylthio)pyrimido[4,5-5γ,5δ]-(4ζ-tert-butyl)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-methylaminopyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-methylaminopyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-methylaminopyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-methylaminopyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-methylaminopyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-methylaminopyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Methylaminopyrimido[4,5-5γ,5δ]-(4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methylaminopyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methylaminopyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-

ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methylaminopyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methylaminopyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Methylaminopyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Methylaminopyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Methylaminopyrimido[4,5-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-methylsulphonylpyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-methylsulphonylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-methylsulphonylpyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-methylsulphonylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-methylpropen-1-yl)-2"-methylsulphonyl-pyrimido[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-methylpropen-1-yl)-2"-methylsulphonyl-pyrimido[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-methylsulphonylpyrimido[4,5-5γ,5δ]-(4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-methylsulphonylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-methylsulphonylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-methylsulphonylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-methylsulphonylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-methylsulphonylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-methylsulphonylpyrimido[4,5-5γ,5δ]-(4ζ-methyl)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-methylsulphonylpyrimido[4,5-5γ,5δ](4ζ-tert-butyl)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-(4-aminophenyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-(4-aminophenyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-(4-aminophenyl)pyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-(4-aminophenyl)pyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(4-aminophenyl)-pyrimido[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-(4-aminophenyl)-pyrimido[4,5-5γ,5δ](4ζ-methylamino)-

(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Aminophenyl)pyrimido[4,5-5γ,5δ]-(4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Aminophenyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Aminophenyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Aminophenyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Aminophenyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(4-Aminophenyl)pyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-(4-Aminophenyl)pyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-(4-Aminophenyl)pyrimido[4,5-5γ,5δ](4ζ-tert-butyl)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-trifluoromethylpyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-trifluoromethylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-trifluoromethylpyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-trifluoromethylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-trifluoromethyl-

pyrimido[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-trifluoromethyl-pyrimido[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethyl-amino)pristinamycin I_E

· 2"-Trifluoromethylpyrimido[4,5-5γ,5δ]-(4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Trifluoromethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Trifluoromethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Trifluoromethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Trifluoromethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Trifluoromethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Trifluoromethylpyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Trifluoromethylpyrimido[4,5-5γ,5δ](4ζ-tert-butyl)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-cyclopropylpyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-cyclopropylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-cyclopropylpyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-cyclopropylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-cyclopropylpyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-cyclopropylpyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-cyclopropylpyrimido[4,5-5γ,5δ]-(4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-cyclopropylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-cyclopropylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-cyclopropylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-cyclopropylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-cyclopropylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-cyclopropylpyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-cyclopropylpyrimido[4,5-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-morpholinomethylpyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-morpholinomethylpyrimido-

[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-Allyl-2"-morpholinomethylpyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-morpholinomethylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-morpholinomethyl-pyrimido[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-morpholinomethyl-pyrimido[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethyl-amino)pristinamycin I_E

· 2"-Morpholinomethylpyrimido[4,5-5γ,5δ]-(4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Morpholinomethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Morpholinomethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Morpholinomethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Morpholinomethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Morpholinomethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Morpholinomethylpyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Morpholinomethylpyrimido[4,5-5γ,5δ](4ζ-tert-butyl)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-ethylpyrimido[4,5-5γ,5δ]pristinamycin I_E

· 4ε-Bromo-2"-ethylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-ethylpyrimido[4,5-5γ,5δ]pristinamycin I_E

· 4ε-Allyl-2"-ethylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-ethylpyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-ethylpyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Ethylpyrimido[4,5-5γ,5δ](4ζ-diethylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Ethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Ethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Ethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Ethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Ethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-

pristinamycin I_E

· 2"-Ethylpyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Ethylpyrimido[4,5-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-propylpyrimido[4,5-5γ,5δ]pristinamycin I_E

· 4ε-Bromo-2"-propylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-propylpyrimido[4,5-5γ,5δ]pristinamycin I_E

· 4ε-Allyl-2"-propylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-propylpyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-propylpyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Propylpyrimido[4,5-5γ,5δ](4ζ-diethylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Propylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Propylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Propylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Propylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-

pristinamycin I_E

· 2"-Propylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Propylpyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Propylpyrimido[4,5-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-isopropylpyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Bromo-2"-isopropylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Allyl-2"-isopropylpyrimido[4,5-5γ,5δ]-pristinamycin I_E

· 4ε-Allyl-2"-isopropylpyrimido[4,5-5γ,5δ]-(4ζ-methylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-isopropylpyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-isopropylpyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Isopropylpyrimido[4,5-5γ,5δ](4ζ-diethylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Isopropylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Isopropylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Isopropylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-

propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Isopropylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Isopropylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Isopropylpyrimido[4,5-5γ,5δ](4ζ-methyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Isopropylpyrimido[4,5-5γ,5δ](4ζ-tert-butyl)-(4ζ-dedimethylamino)pristinamycin I_E

· 4ε-Bromo-2"-cyclopropylaminomethylpyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-Bromo-2"-cyclopropylaminomethylpyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-Allyl-2"-cyclopropylaminomethylpyrimido-[4,5-5γ,5δ]pristinamycin I_E

· 4ε-Allyl-2"-cyclopropylaminomethylpyrimido-[4,5-5γ,5δ](4ζ-methylamino)(4ζ-dedimethylamino)-pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-cyclopropylamino-methylpyrimido[4,5-5γ,5δ]pristinamycin I_E

· 4ε-(2-Methylpropen-1-yl)-2"-cyclopropylamino-methylpyrimido[4,5-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Cyclopropylaminomethylpyrimido[4,5-5γ,5δ](4ζ-diethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Cyclopropylaminomethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-allylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Cyclopropylaminomethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-ethylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Cyclopropylaminomethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-propylamino)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Cyclopropylaminomethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(4-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Cyclopropylaminomethylpyrimido[4,5-5γ,5δ](4ζ-N-methyl-N-(3-pyridylmethyl)amino)(4ζ-dedimethylamino)-pristinamycin I_E

· 2"-Cyclopropylaminomethylpyrimido[4,5-5γ,5δ]-(4ζ-methyl)(4ζ-dedimethylamino)pristinamycin I_E

· 2"-Cyclopropylaminomethylpyrimido[4,5-5γ,5δ]-(4ζ-tert-butyl)(4ζ-dedimethylamino)pristinamycin I_E

PREPARATION OF THE INTERMEDIATES

Example A

Method a

170 mg of pristinamycin I_B dissolved in 0.5 cm^3 of dry dimethylformamide are placed in a three-necked flask maintained under a nitrogen atmosphere, and then 0.026 cm^3 of 3,3-dimethylallyl bromide dissolved in 0.2 cm^3 of dry dimethylformamide is added. After stirring for 3 hours at room temperature, the reaction mixture is diluted with 10 cm^3 of distilled water and then washed with twice 20 cm^3 of ethyl

acetate. The organic phase is decanted off, washed with water, dried over magnesium sulphate, filtered and then concentrated under reduced pressure (2.7 kPa) to give a solid which is taken up in ethyl ether and then dried. The solid is purified by flash chromatography (eluent: dichloromethane-methanol 97/3) to give 57 mg of 4-N-(2-methyl-2-buten-4-yl)pristinamycin I_B in the form of a pale-yellow solid melting at 170°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 1.70 (s, 6H : CH_3); 2.85 (s, 3H : $ArNCH_3$); 2.87 (mt, 1H : 1H of CH_2 at position 4β); 3.23 (s, 3H : NCH_3); 3.30 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 3.82 and 3.91 (2 dd, J = 16.5 and 5 Hz, 1H each : $ArNCH_2$); 5.08 (mt, 1H : CH=); 5.18 (dd, J = 12 and 4 Hz, 1H : 4α); 6.62 (d, J = 8.5 Hz, 2H : aromatic H at position 4ε); 7.03 (d, J = 8.5 Hz, 2H : aromatic H at position 4δ).

Method b

660 mg of pristinamycin I_B dissolved in 3.3 cm^3 of dry chloroform (over amylene) are placed in a three-necked flask maintained under a nitrogen atmosphere, and then 65 mg of $NaHCO_3$ powder are added. After stirring for one hour, 0.09 cm^3 of 3,3-dimethylallyl bromide dissolved in 0.9 cm^3 of dry chloroform (over amylene) is added. After stirring for 18 hours at room temperature, the reaction mixture is diluted with 20 cm^3 of chloroform and then washed with 3 times 5 cm^3 of distilled water. The organic phase is

decanted off, dried over magnesium sulphate, filtered and then concentrated under reduced pressure (2.7 kPa) to give a solid which is taken up in 20 cm^3 of ether and then dried. This solid is purified by flash chromatography (eluent: dichloromethane-methanol 97/3) to give 360 mg of 4-N-(2-methyl-2-buten-4-yl)-pristinamycin I_B in the form of a pale-yellow solid melting at 170°C.

Example B

1.7 g of pristinamycin I_B in 5.1 cm^3 of dry dimethylformamide are placed in a three-necked flask maintained under a nitrogen atmosphere, and then 310 mg of crotyl bromide are added. The mixture is stirred for 22 hours at room temperature. The reaction mixture is diluted with 50 cm^3 of distilled water, with stirring, and then extracted with twice 20 cm^3 of ethyl acetate. The aqueous phase is decanted off and the organic phase is washed with twice 10 cm^3 of distilled water, decanted off, dried over magnesium sulphate, filtered and then concentrated under reduced pressure (2.7 kPa) to give 1.1 g of a yellow oil which is purified by flash chromatography (eluent: dichloromethane-methanol 97/3) to give 0.62 g of 4-N-(2-butenyl)pristinamycin I_B in the form of a white solid melting at 180°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 1.70 (d, J = 6 Hz, 3H : CH_3); from 2.85 to 2.90 (mt, 1H : 1H of CH_2 at position 4β); 2.90 (s, 3H : $ArNCH_3$); 3.28 (s, 3H : NCH_3); 3.32 (t, J = 12 Hz, 1H : the other

H of CH_2 at position 4β); 3.81 and 3.91 (2 broad d, J = 18 Hz, 1H each : $ArNCH_2$); 5.22 (dd, J = 12 and 4 Hz, 1H : 4α); 5.43 and 5.57 (d mt and dq respectively, J = 14 Hz and J = 14 and 6 Hz, 1H each : CH=CH); 6.62 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 7.05 (d, J = 8 Hz, 2H : aromatic H at position 4δ).

Example C

By carrying out the procedure as in Example A but starting with 2.5 g of pristinamycin I_B, 400 mg of bromoacetic acid in 8 cm^3 of dry dimethylformamide, 2.1 g of a white solid are obtained after stirring for 48 hours at room temperature, which solid is purified by flash chromatography (successive eluents: dichloromethane-methanol 95/5 then 90/10 then 80/20) to give 1.1 g of an oil which is taken up in dichloromethane, acidified to pH 4 with acetic acid and then washed with distilled water.

The organic phase is decanted off, dried over magnesium sulphate, filtered and then concentrated under reduced pressure (2.7 kPa), and then taken up in diethyl ether to give 750 mg of 4-N-(carboxymethyl)-pristinamycin I_B in the form of a white solid melting at 230°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 2.85 (dd, J = 12 and 4 Hz, 1H : 1H of CH_2 at position 4β); 3.03 (s, 3H : $ArNCH_3$); from 3.10 to 3.40 (mt, 1H : the other H of CH_2 at position 4β); 3.25 (s, 3H : NCH_3); 4.04 (limiting AB, J = 18 Hz, 2H : $ArNCH_2$); 5.25 (dd,

J = 12 and 4 Hz, 1H : 4α); 6.62 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 7.07 (d, J = 8 Hz, 2H : aromatic H at position 4δ).

Example D

By carrying out the procedure as in Example A but starting with 1 g of pristinamycin I_B, 0.1 ml of allyl bromide in 3 cm^3 of dry dimethylformamide, 620 mg of a white solid are obtained after stirring for 72 hours at room temperature, which solid is purified by flash chromatography (eluent: dichloromethane-methanol 97/3) to give 290 mg of 4-N-allylpristinamycin I_B in the form of a white-yellow solid melting at 208°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 2.88 (dd, J = 12 and 4 Hz, 1H : 1H of CH_2 at position 4β); 2.90 (s, 3H : $ArNCH_3$); 3.21 (s, 3H : NCH_3); 3.29 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 3.85 and 3.95 (2 broad d, J = 18 Hz, 1H each : $ArNCH_2$); 5.10 and 5.17 (2 d respectively, J = 17 Hz and J = 11.5 Hz, 1H each : $=CH_2$); 5.20 (dd, J = 12 and 4 Hz, 1H : 4α); 5.78 (mt, 1H : CH=); 6.60 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 7.02 (d, J = 8 Hz, 2H : aromatic H at position 4δ).

Example E

By carrying out the procedure as in Example A but starting with 1 g of pristinamycin I_B in 3 cm^3 of dry dimethylformamide and 230 mg of cinnamyl bromide, 0.8 g of a white solid is obtained after 72 hours at room temperature, which solid is purified by flash

chromatography (eluent: dichloromethane-methanol 97/3) to give 0.31 g of 4-N-cinnamylpristinamycin I_B in the form of a white solid melting at 204°C.

^{1}H NMR spectrum (600 MHz, $CDCl_3$, δ in ppm): 2.90 (dd, J = 12.5 and 4 Hz, 1H : 1H of CH_2 at position 4β); 2.97 (s, 3H : $ArNCH_3$); 3.24 (s, 3H : NCH_3); 3.33 (t, J = 12.5 Hz, 1H : the other H of CH_2 at position 4β); 4.70 (limiting AB, J = 18 and 5.5 Hz, 2H : $ArNCH_2$); 5.20 (dd, J = 12.5 and 4 Hz, 1H : 4α); 6.23 and 6.52 (broad d and dt respectively, J = 16.5 and 5.5 Hz and J = 16.5 Hz, 1H each : CH=CH); 6.68 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 7.07 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.25 to 7.40 (mt, 5H : aromatic H of phenyl).

Example F

By carrying out the procedure as in Example A but starting with 1 g of pristinamycin I_B in 3 cm^3 of dry dimethylformamide and 240 mg of benzyl bromide, 0.85 g of a white solid is obtained after 72 hours at room temperature, which solid is purified by flash chromatography (eluent: dichloromethane-methanol 97/3) to give 0.64 g of 4-N-benzylpristinamycin I_B in the form of a white solid melting at a temperature greater than 260°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 2.86 (dd, J = 12.5 and 4 Hz, 1H : 1H of CH_2 at position 4β); 3.10 (s, 3H : $ArNCH_3$); 3.26 (s, 3H : NCH_3); 3.32 (t, J = 12.5 Hz, 1H : the other H of CH_2 at position

4β); 4.52 and 4.69 (2 d, J = 18 Hz, 1H each : $ArNCH_2$); 5.16 (dd, J = 12.5 and 4 Hz, 1H : 4α); 6.59 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 7.01 (d, J = 8 Hz, 2H : aromatic H at position 4δ); 7.18 (mt, 2H : H at the ortho position of the benzyl); 7.28 (mt, 2H : H at the meta position of the benzyl); 7.40 (t, J = 7.5 Hz, 1H : H at the para position of the benzyl).

Example G

By carrying out the procedure as in Example A but starting with 1 g of pristinamycin I_B in 3 cm^3 of dry dimethylformamide and 200 mg of ethyl iodide, 0.65 g of a pale-yellow solid is obtained after 5 hours at 60°C and then 72 hours at room temperature and after adding an additional 20 mg of ethyl iodide and heating at 60°C for 4 hours, which solid is purified by flash chromatography (eluent: dichloromethane-methanol 97/3) to give 0.37 g of 4-N-ethylpristinamycin I_B in the form of a white solid melting at a temperature greater than 260°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 1.10 (t, J = 7 Hz, 3H : CH_3 of ethyl); 2.87 (s, 3H : $ArNCH_3$); 2.90 (dd, J = 12.5 and 4 Hz, 1H : 1H of CH_2 at position 4β); 3.25 (s, 3H : NCH_3); 3.32 (t, J = 12.5 Hz, 1H : the other H of CH_2 at position 4β); 3.39 (mt, 2H : $ArNCH_2$); 5.21 (dd, J = 12.5 and 4 Hz, 1H : 4α); 6.60 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 7.04 (d, J = 8 Hz, 2H : aromatic H at position 4δ).

Example H

1 g of pristinamycin I_B in 3 cm^3 of dry dimethylformamide is placed in a three-necked flask maintained under a nitrogen atmosphere, and then 175 mg of a mixture of about 20% 4-bromo-1-butene, 15% of bromomethylcyclopropane and 65% of bromocyclobutane and 195 mg of sodium iodide are added. The mixture is stirred for 72 hours at room temperature and then heated for 7 hours at 60°C. 175 mg of this mixture are again added and then the stirring is continued for 48 hours. The reaction mixture is diluted with 50 cm^3 of distilled water, with stirring, and then extracted with twice 20 cm^3 of ethyl acetate. The aqueous phase is decanted off and then the organic phase is washed with twice 10 cm^3 of distilled water, decanted off, dried over magnesium sulphate, filtered and then concentrated under reduced pressure (2.7 kPa) to give 800 mg of a white powder which is purified by flash chromatography (eluent: dichloromethane-methanol 98/2) and then by high-performance liquid chromatography (HPLC) to give 220 mg of 4-N-(but-2-enyl)pristinamycin I_B in the form of a white solid melting at 190°C.

^1H NMR spectrum (300 MHz, $CDCl_3$, δ in ppm): 2.29 (mt, 2H : CH_2); 2.88 (dd, J = 12 and 4 Hz, 1H : 1H of CH_2 at position 4β); 2.90 (s, 3H : $ArNCH_3$); 3.25 (s, 3H : NCH_3); 3.31 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 3.38 (mt, 2H : $ArNCH_2$); 5.05 and 5.10 (2 dd, respectively J = 10.5 and 2 Hz and J = 16.5 and

2 Hz, 1H each : $=CH_2$); 5.20 (dd, J = 12 and 4 Hz, 1H : 4α); 5.78 (mt, 1H : CH=); 6.62 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 7.04 (d, J = 8 Hz, 2H : aromatic H at position 4δ).

Example I

1 g of pristinamycin I_B in 3 cm^3 of dry dimethylformamide is placed in a three-necked flask maintained under a nitrogen atmosphere, and then 175 mg of a mixture of about 20% 4-bromo-1-butene, 15% of bromomethylcyclopropane and 65% of bromocyclobutane and 195 mg of sodium iodide are added. The mixture is stirred for 72 hours at room temperature and then heated for 7 hours at 60°C. 175 mg of this mixture are again added and then the stirring is continued for 48 hours. The reaction mixture is diluted with 50 cm^3 of distilled water, with stirring, and then extracted with twice 20 cm^3 of ethyl acetate. The aqueous phase is decanted off and then the organic phase is washed with twice 10 cm^3 of distilled water, decanted off, dried over magnesium sulphate, filtered and then concentrated under reduced pressure (2.7 kPa) to give 800 mg of a white powder which is purified by flash chromatography (eluent: dichloromethane-methanol 98/2) and then by HPLC chromatography to give 222 mg of 4-N-cyclopropylmethylpristinamycin I_B in the form of a white solid melting at 190°C.

^1H NMR spectrum (300 MHz, $CDCl_3$, δ in ppm): 0.20 and 0.53 (2 mts, 2H each : CH_2 of cyclopropane);

0.92 (mt, 1H : CH of cyclopropane); 2.90 (dd, J = 12.5 and 4 Hz, 1H : 1H of CH_2 at position 4β); 2.93 (s, 3H : $ArNCH_3$); 3.13 and 3.25 (dd and mt respectively, J = 15 and 7 Hz, 1H each : $ArNCH_2$); 3.25 (s, 3H : NCH_3); 3.32 (t, J = 12.5 Hz, 1H : the other H of CH_2 at position 4β); 5.20 (dd, J = 12.5 and 4 Hz, 1H : 4α); 6.67 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 7.04 (d, J = 8 Hz, 2H : aromatic H at position 4δ).

Example J

2 g of pristinamycin I_B in 10 cm^3 of dry dimethylformamide are placed in a three-necked flask maintained under a nitrogen atmosphere, and then 460 mg of 4-chloromethylpyridine hydrochloride and 350 mg of sodium iodide are added. The mixture is stirred for 5 hours at 60°C. The reaction mixture is poured over 150 cm^3 of distilled water and then extracted with 3 times 100 cm^3 of ethyl acetate. The aqueous phase is decanted off and then the organic phase dried over magnesium sulphate, filtered and then concentrated under reduced pressure (2.7 kPa) to give 2.6 g of a yellow oil which is purified by 2 flash chromatographies (eluent: dichloromethane-methanol 97/3) to give 130 mg of 4-N-(4-pyridylmethyl)-pristinamycin I_B in the form of a white solid melting at 260°C.

^1H NMR spectrum (300 MHz, $CDCl_3$, δ in ppm): 2.90 (dd, J = 12.5 and 4 Hz, 1H : 1H of CH_2 at position 4β); 3.07 (s, 3H : $ArNCH_3$); 3.27 (s, 3H : NCH_3); 3.32

(t, J = 12.5 Hz, 1H : the other H of CH_2 at position 4β); 4.50 and 4.63 (2 d, J = 17 HzHz, 1H each : $ArNCH_2$); 5.16 (dd, J = 12.5 and 4 Hz, 1H : 4α); 6.59 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 7.01 (d, J = 8 Hz, 2H : aromatic H at position 4δ); 7.13 (d, J = 5.5 Hz; 2H : H at position β of pyridine); 8.60 (d, J = 5.5 Hz; 2H : H at position α of pyridine).

Example K

By carrying out the procedure as in Example A but starting with 1 g of pristinamycin I_B in 3 cm^3 of dry dimethylformamide and 237 mg of iodobutane, 0.94 g of a pale-yellow solid is obtained after 48 hours at 60°C and then 72 hours at room temperature, which solid is purified by flash chromatography (eluent: dichloromethane-methanol 98/2) to give 0.23 g of Hz4-N-butylpristinamycin I_B in the form of a white solid melting at 170°C.

^1H NMR spectrum (300 MHz, $CDCl_3$, δ in ppm): 0.95 (t, J = 7.5 Hz, 3H : CH_3 of butyl); 1.35 and 1.55 (2 mts, 2H each : CH_2CH_2 of butyl); 2.90 (s, 3H : $ArNCH_3$); 2.90 (dd, J = 12.5 and 4 Hz, 1H : 1H of CH_2 at position 4β); from 3.20 to 3.40 (mt, 3H : the other H of CH_2 at position 4β and $ArNCH_2$); 3.28 (s, 3H : NCH_3); 5.21 (dd, J = 12.5 and 4 Hz, 1H : 4α); 6.60 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 7.05 (d, J = 8 Hz, 2H : aromatic H at position 4δ).

Example L

By carrying out the procedure as in Example A

but starting with 3 g of pristinamycin I_B in 15 cm^3 of dry dimethylformamide and 720 mg of iodopropane, 2.07 g of a pale-yellow oil are obtained after 22 hours at 50°C, which oil is purified by 2 flash chromatographies (eluent: dichloromethane-methanol 98/2 and dichloromethane-methanol 99/1) to give 0.49 g of 4-N-propylpristinamycin I_B in the form of a white solid melting at 220°C (dec.).

^{1}H NMR spectrum (300 MHz, $CDCl_3$, δ in ppm): 0.95 (t, J = 7.5 Hz, 3H : CH_3 of propyl); 1.58 (mt, 2H : CH_2 of propyl); 2.88 (mt, 1H : 1H of CH_2 at position 4β); 2.90 (s, 3H : $ArNCH_3$); from 3.15 to 3.40 (mt, 3H : the other H of CH_2 at position 4β and $ArNCH_2$); 3.25 (s, 3H : NCH_3); 5.20 (dd, J = 12.5 and 4 Hz, 1H : 4α); 6.60 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 7.03 (d, J = 8 Hz, 2H : aromatic H at position 4δ).

Example M

By carrying out the procedure as in Example A but starting with 2 g of pristinamycin I_B in 5 cm^3 of dry dimethylformamide and 480 mg of 2-iodopropane, 2.07 g of a pale-yellow oil are obtained after 6 hours at 60°C and then 17 hours at room temperature, which oil is purified by flash chromatography (eluent: dichloromethane-methanol 97/3) to give 0.19 g of 4-N-isopropylpristinamycin I_B in the form of a white solid melting at 220°C (dec.).

^{1}H NMR spectrum (300 MHz, $CDCl_3$, δ in ppm): 1.14 and 1.17 (2 d, J = 6.5 Hz, 6H : CH_3 of isopropyl);

2.68 (s, 3H : $ArNCH_3$); 2.88 (dd, J = 12 and 4 Hz, 1H : 1H of CH_2 at position 4β); 3.23 (s, 3H : NCH_3); 3.30 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 3.90 (mt, 1H : ArNCH); 5.20 (dd, J = 12 and 4 Hz, 1H : 4α); 6.68 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 7.03 (d, J = 8 Hz, 2H : aromatic H at position 4δ).

Example N

By carrying out the procedure as in Example A but starting with 3 g of pristinamycin I_B in 15 cm^3 of dry dimethylformamide and 780 mg of 3-methyl-2-propane iodide, 3.86 g of a solid are obtained after 70 hours at room temperature and then addition of an additional 160 mg of 3-methyl-2-propane iodide and heating at 50°C for 24 hours, which solid is purified by flash chromatography (eluent: dichloromethane-methanol 98/2) to give 690 mg of 4-N-isobutylpristinamycin I_B in the form of a white solid melting at 190°C (dec.).

^1H NMR spectrum (300 MHz, $CDCl_3$, δ in ppm): 0.93 (d, J = 7 Hz, 6H : CH_3 of isobutyl); 2.05 (mt, 1H : CH of isobutyl); 2.92 (dd, J = 12.5 and 4 Hz, 1H : 1H of CH_2 at position 4β); 2.98 (s, 3H : $ArNCH_3$); 3.10 and 3.18 (2 dd, J = 15 and 7.5 Hz, 1H each : $ArNCH_2$); 3.30 (s, 3H : NCH_3); 3.35 (t, J = 12.5 Hz, 1H : the other H of CH_2 at position 4β); 5.20 (dd, J = 12.5 and 4 Hz, 1H : 4δ); 6.60 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 7.03 (d, J = 8 Hz, 2H : aromatic H at position 4δ).

Example O

3 g of pristinamycin I_B in 15 cm^3 of dry dimethylformamide are placed in a three-necked flask maintained under a nitrogen atmosphere, and then 690 mg of 3-chloromethylpyridine hydrochloride and 350 mg of sodium iodide are added. The mixture is stirred for 24 hours at 60°C and then for 48 hours at room temperature. The reaction mixture is poured over 50 cm^3 of distilled water supplemented with sodium bicarbonate and then extracted with 3 times 50 cm^3 of ethyl acetate. The aqueous phase is decanted off and then the organic phase dried over magnesium sulphate, filtered and then concentrated under reduced pressure (2.7 kPa) to give 2.96 g of a yellow solid which is purified by flash chromatography (eluent: dichloromethane-methanol 98/2) to give 409 mg of 4-N-(3-pyridylmethyl)pristinamycin I_B in the form of a white solid melting at 186°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 2.87 (dd, J = 12.5 and 4 Hz, 1H : 1H of CH_2 at position 4β); 3.05 (s, 3H : $ArNCH_3$); 3.23 (s, 3H : NCH_3); 3.29 (t, J = 12.5 Hz, 1H : the other H of CH_2 at position 4β); 4.50 and 4.65 (2 d, J = 18 Hz, 1H each : $ArNCH_2$); 5.15 (dd, J = 12.5 and 4 Hz, 1H : 4α); 6.62 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 7.05 (d, J = 8 Hz, 2H : aromatic H at position 4δ); 7.35 (mt, 1H : H at position 5 of pyridine); 7.42 (broad d, J = 8 Hz, 1H : H at position 4 of pyridine); 8.45 (broad d, J = 5 Hz, 1H : H at position 6 of pyridine);

8.58 (broad s, 1H : H at position 2 of pyridine).

Example P

3 g of pristinamycin I_B in 15 cm^3 of dry dimethylformamide are placed in a three-necked flask maintained under a nitrogen atmosphere, and then 690 mg of 2-chloromethylpyridine hydrochloride and 70 mg of sodium iodide are added. The mixture is stirred for 2 hours at 60°C and then an additional 0.48 g of sodium iodide is added and the stirring is maintained for 23 hours at 60°C. The reaction mixture is poured over 150 cm^3 of distilled water supplemented with sodium bicarbonate and then extracted with 3 times 100 cm^3 of ethyl acetate. The aqueous phase is decanted off and then the organic phases are pooled and then washed with an aqueous solution of sodium sulphite. The organic phase is decanted off, dried over magnesium sulphate, filtered and then concentrated under reduced pressure (2.7 kPa) to give 3.34 g of a yellow solid which is purified by flash chromatography (eluent: dichloromethane-methanol 98/2) to give 1.16 g of 4-N-(2-pyridylmethyl)pristinamycin I_B in the form of a white solid melting at 190°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 2.85 (dd, J = 12.5 and 4 Hz, 1H : 1H of CH_2 at position 4β); 3.15 (s, 3H : $ArNCH_3$); 3.24 (s, 3H : NCH_3); 3.29 (t, J = 12.5 Hz, 1H : the other H of CH_2 at position 4β); 4.55 and 4.83 (2 d, J = 18 Hz, 1H each : $ArNCH_2$); 5.10 (dd, J = 12.5 and 4 Hz, 1H : 4α); 6.57 (d,

J = 8 Hz, 2H : aromatic H at position 4ε); 6.99 (mt, 1H : H at position 3 of pyridine); 7.00 (d, J = 8 Hz, 2H : aromatic H at position 4δ); 7.08 (dd, J = 7.5 and 5 Hz; 1H : H at position 5 of pyridine); 7.80 (dt, J = 7.5 and 1 Hz, 1H : H at position 4 of pyridine); 8.57 (broad d, J = 5 Hz; 1H : H at position 6 of pyridine).

Example Q

5 g of pristinamycin I_B in 7 cm^3 of dry dimethylformamide are placed in a three-necked flask maintained under a nitrogen atmosphere, and then 0.66 g of 1-chloro-3-hydroxypropane, 50 mg of sodium iodide and 580 mg of potassium bicarbonate are added. The mixture is stirred for 22 hours at 70°C. The reaction mixture is cooled, poured over 30 cm^3 of distilled water and then extracted with 3 times 40 cm^3 of ethyl acetate. The aqueous phase is decanted off and then the organic phase dried over magnesium sulphate, filtered and then concentrated under reduced pressure (2.7 kPa) to give 5.41 g of a solid which is purified by flash chromatography (eluent: dichloromethane-methanol 98/2) to give 0.28 g of 4-N-(3-hydroxy-3-propyl)pristinamycin I_B in the form of a white solid melting at 186°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 1.75 (mt, 2H : central CH_2 of propyl); 2.88 (mt, 1H : 1H of CH_2 at position 4β); 2.90 (s, 3H : $ArNCH_3$); 3.24 (s, 3H : NCH_3); 3.30 (t, J = 12.5 Hz, 1H : the other H of CH_2 at position 4β); 3.43 and 3.62 (2 mts, 2H each :

$ArNCH_2$ and CH_2O); 5.20 (dd, J = 12.5 and 4 Hz, 1H : 4α); 6.68 (unresolved complex, 2H : aromatic H at position 4ε); 7.03 (d, J = 8 Hz, 2H : aromatic H at position 4δ).

Example R

By carrying out the procedure as in Example Q but starting with 4 g of pristinamycin I_B, 1.7 cm^3 of 3-(dioxo-1,2-ethylene)bromopropane in 12 cm^3 of dry dimethylformamide, 3.8 g of a yellow solid are obtained after heating for 24 hours at 60°C, which solid is purified by flash chromatography (eluent: dichloromethane-methanol 97/3) to give 0.81 g of 4-N-[2-(1,3-dioxolan-2-yl)ethyl]pristinamycin I_B in the form of a white solid melting at a temperature greater than 260°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 1.91 (mt, 2H : central CH_2); 2.87 (s, 3H : $ArNCH_3$); 2.88 (dd, J = 12 and 4 Hz, 1H : 1H of CH_2 at position 4β); 3.25 (s, 3H : NCH_3); 3.29 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 3.35 to 3.55 (mt, 2H : $ArNCH_2$); 3.87 and 3.97 (2 mts, 2H each : OCH_2CH_2O); 4.92 (t, J = 4 Hz, 1H : OCHO); 5.21 (dd, J = 12 and 4 Hz, 1H : 4α); 6.64 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 7.04 (d, J = 8 Hz, 2H : aromatic H at position 4δ).

Example S

By carrying out the procedure as in Example A but starting with 0.53 g of 4ε-chloropristinamycin I_B,

0.082 cm^3 of allyl bromide in 3 cm^3 of dry dimethylformamide, a solid is obtained after 7 hours at 50°C and then addition of an additional 0.5 cm^3 of allyl bromide and heating for 2 hours 30 minutes, which solid is purified by flash chromatography (eluent: dichloromethane-methanol 98/2) to give 77 mg of 4-N-allyl-4ε-chloropristinamycin I_B in the form of a very light yellow solid melting at 175°C (dec.).

^1H NMR spectrum (300 MHz, $CDCl_3$, δ in ppm): 2.71 (s, 3H : $ArNCH_3$); 2.93 (dd, J = 12 and 4 Hz, 1H : 1H of CH_2 at position 4β); 3.21 (s, 3H : NCH_3); 3.33 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 3.58 (d, J = 6 Hz, 2H : $ArNCH_2$); 5.20 and 5.27 (2 dd, respectively J = 11 and 1 Hz and J = 16 and 1 Hz, 1H each : $=CH_2$); 5.30 (dd, J = 12 and 4 Hz, 1H : 4α); from 5.75 to 5.95 (mt, 1H : CH=); 6.95 (d, J = 8 Hz, 1H : aromatic H at position 4ε); 7.03 (dd, J = 8 and 1.5 Hz, 1H : aromatic H at position 4δ); 7.18 (d, J = 1.5 Hz, 1H : aromatic H at position 4δ and at the ortho position with respect to the Cl).

4ε-Chloropristinamycin I_B may be prepared as described in Patent Application EP 772630.

Example T

0.3 g of 4-N-ethoxycarbonylmethyl-pristinamycin I_B in 3.5 cm^3 of dichloromethane is placed in a round-bottomed flask and then 51 mg of N-chlorosuccinimide are added. The mixture is stirred for 5 days at room temperature. The reaction mixture is

concentrated to dryness under reduced pressure (2.7 kPa) at 30°C. The solid obtained is stirred 3 times in 5 cm^3 of distilled water, filtered, washed with 3 times 3 cm^3 of ether to give a yellow solid which is recrystallized from 4 cm^3 of ethanol. After filtration of the crystals and drying under reduced pressure (135 Pa) at 50°C, 0.15 g of 4ε-chloro-(4-N-ethoxycarbonylmethyl)pristinamycin I_B is obtained in the form of light beige crystals melting at 176°C.

^1H NMR spectrum (300 MHz, $CDCl_3$, δ in ppm): 1.34 (t, J = 7 Hz, 3H : CH_3 of ethyl); 2.95 (dd, J = 12 and 4 Hz, 1H : 1H of CH_2 at position 4β); 3.05 (s, 3H : $ArNCH_3$); 3.32 (s, 3H : NCH_34); 3.38 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 3.85 and 4.19 (2 d, J = 17.5 Hz, 1H each : $ArNCH_2$); 4.22 (q, J = 7 Hz, 2H : CH_2 of ethyl); 5.29 (dd, J = 12 and 4 Hz, 1H : 4α); 7.10 (d, J = 8.5 Hz, 1H : aromatic H at position 4ε); 7.25 (mt, 2H : aromatic H at position 4δ).

4-N-Ethoxycarbonylmethylpristinamycin I_B may be prepared as described below in Example AD.

Example U

By carrying out the procedure as in Example T but starting with 0.3 g of 4-N-ethylpristinamycin I_B and 0.545 g of N-chlorosuccinimide in 3.5 cm^3 of dichloromethane, 0.33 g of a solid is obtained after stirring for one week at room temperature, which solid is recrystallized from 6 cm^3 of ethanol. After filtration of the crystals and drying under reduced

pressure (135 Pa) at 50°C, 0.15 g of 4ε-chloro-4-N-ethylpristinamycin I_B is obtained in the form of light beige crystals melting at > 260°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 1.16 (t, J = 7 Hz, 3H : CH_3 of ethyl); 2.70 (s, 3H : $ArNCH_3$); 2.92 (dd, J = 12 and 4 Hz, 1H : 1H of CH_2 at position 4β); 3.00 (q, J = 7 Hz, 2H : NCH_2 of ethyl); 3.22 (s, 3H : NCH_3); 3.33 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 5.22 (dd, J = 12 and 4 Hz, 1H : 4α); 6.95 (d, J = 8 Hz, 1H : aromatic H at position 4ε); 7.03 (dd, J = 8 and 1.5 Hz, 1H : aromatic H at position 4δ); 7.23 (d, J = 1.5 Hz, 1H : aromatic H at position 4δ and at the ortho position with respect to the Cl).

Example V

By carrying out the procedure as in Example T but starting with 200 mg of 4-N-isobutylpristinamycin I_B, 44 mg of N-chlorosuccinimide and 3 cm^3 of dichloromethane, 99 mg of a white solid are obtained after stirring for 36 hours at room temperature and then for 40 minutes under reflux, which solid is stirred in 10 cm^3 of water, filtered and then rinsed to give 690 mg of 4-N-isobutylpristinamycin I_B in the form of a white solid melting at 190°C (dec.).

^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.88 (d, J = 7 Hz, 6H : CH_3 of isobutyl); 1.80 (mt, 1H : CH of isobutyl); 2.69 (s, 3H : $ArNCH_3$); 2.75 (limiting AB, 2H : $ArNCH_2$); 2.95 (dd, J = 12 and 4 Hz, 1H : 1H of

CH_2 at position 4β); 3.25 (s, 3H : NCH_3); 3.34 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 5.27 (dd, J = 12 and 4 Hz, 1H : 4α); 6.99 (d, J = 8 Hz, 1H : aromatic H at position 4ε); 7.06 (broad d, J = 8 Hz, 1H : aromatic H at position 4δ); from 7.25 to 7.40 (mt, 1H : aromatic H at position 4δ and at the ortho position with respect to the Cl).

Example W

By carrying out the procedure as in Example T but starting with 224 mg of 4-N-(4-pyridylmethyl)-pristinamycin I_B, 32 mg of N-chlorosuccinimide and 3 cm^3 of acetonitrile, a beige solid is obtained after stirring for 2 hours at 65°C, which solid is stirred in 10 cm^3 of water, filtered and then rinsed and then purified by flash chromatography (eluent: dichloromethane-methanol 98/2) to give 190 mg of 4ε-chloro-4-N-pyridylmethyl)pristinamycin I_B in the form of a white pale-yellow solid melting at 232°C (dec.).

^1H NMR spectrum (300 MHz, $CDCl_3$, δ in ppm): 2.67 (s, 3H : $ArNCH_3$); 2.97 (dd, J = 12.5 and 4 Hz, 1H : 1H of CH_2 at position 4β); 3.24 (s, 3H : NCH_3); 3.32 (t, J = 12.5 Hz, 1H : the other H of CH_2 at position 4β); 4.10 (s, 2H : $ArNCH_2$); 5.29 (dd, J = 12.5 and 4 Hz, 1H : 4α); 6.99 (d, J = 8 Hz, 1H : aromatic H at position 4ε); 7.06 (broad d, J = 8 and 1.5 Hz, 1H : aromatic H at position 4δ); from 7.15 to 7.40 (mt, 1H : aromatic H at position 4δ and at the ortho position with respect to the Cl); 7.37 (d, J = 6 Hz; 2H : H at position β of

pyridine); 8.57 (d, J = 6 Hz; 2H : H at position α of pyridine).

Example X

By carrying out the procedure as in Example T but starting with 260 mg of 4-N-(3-pyridylmethyl)-pristinamycin I_B, 37 mg of N-chlorosuccinimide and 3 cm^3 of acetonitrile, 270 mg of a white solid are obtained after stirring for 20 hours at 65°C, which solid is stirred in 10 cm^3 of water, filtered and then rinsed to give 120 mg of 4ε-chloro-4-N-(3-pyridylmethyl)-pristinamycin I_B in the form of a white solid melting at 258°C (dec.).

^1H NMR spectrum (300 MHz, $CDCl_3$, δ in ppm): 2.65 (s, 3H : $ArNCH_3$); 2.98 (dd, J = 12 and 4 Hz, 1H : 1H of CH_2 at position 4β); 3.23 (s, 3H : NCH_3); 3.33 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 4.13 (s, 2H : $ArNCH_2$); 5.19 (dd, J = 12 and 4 Hz, 1H : 4α); 7.00 (d, J = 8 Hz, 1H : aromatic H at position 4ε); 7.08 (dd, J = 8 and 1.5 Hz, 1H : aromatic H at position 4δ); from 7.15 to 7.40 (mt, 2H : aromatic H at position 4δ and at the ortho position with respect to the Cl and H at position 5 of pyridine); 7.80 (mt, 1H : H at position 4 of pyridine); 8.55 (broad d, J = 6 Hz; 1H : H at position 6 of pyridine); 8.65 (broad s, 1H : H at position 2 of pyridine).

Example Y

2 g of pristinamycin I_B in 6 cm^3 of dry dimethylformamide are placed in a three-necked flask

maintained under a nitrogen atmosphere, and then 1.46 g of 4-pyridylmethyl bromoacetate hydrobromide and 0.33 cm^3 of triethylamine are added. The mixture is stirred for 18 hours at 60°C. The reaction mixture is cooled, poured over 100 cm^3 of distilled water and then extracted with 4 times 30 cm^3 of ethyl acetate. The aqueous phase is decanted off and then the organic phase washed again with 3 times 10 cm^3 of distilled water, decanted off and then dried over magnesium sulphate, filtered and then concentrated under reduced pressure (2.7 kPa) to give 1.2 g of a pale-yellow solid which is purified by flash chromatography (eluent: dichloromethane-methanol 97/3) to give 0.53 g of a solid which is repurified by HPLC to give 197 mg of (4-N-pyridylmethoxycarbonylmethyl)pristinamycin I_B in the form of a white powder melting at 252°C.

4-Pyridylmethyl bromoacetate hydrobromide may be prepared in the following manner:

1.09 g of 4-hydroxymethylpyridine dissolved in 20 cm^3 of chloroform (dry over amylene) are placed in a three-necked flask maintained under a nitrogen atmosphere and then 0.88 cm^3 of bromoacetyl bromide dissolved in 2 cm^3 of chloroform is added over 1 hour at room temperature. After stirring for 24 hours, an additional 10% bromoacetyl bromide is added and then the stirring is continued for 24 hours. The reaction mixture is filtered, taken up in chloroform and then in ether. The resulting solid is dried under reduced

pressure to give 2.1 g of a solid which is used as it is in the next step.

^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 2.92 (dd, J = 12 and 4 Hz, 1H : 1H of CH_2 at position 4β); 3.08 (s, 3H : $ArNCH_3$); 3.27 (s, 3H : NCH_3); 3.33 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 4.17 (s, 2H : $ArNCH_2$); 5.19 (s, 2H : $COOCH_2$); 5.25 (dd, J = 12 and 4 Hz, 1H : 4α); 6.67 (d, J = 8.5 Hz, 2H : aromatic H at position 4ε); 7.07 (d, J = 8.5 Hz, 2H : aromatic H at position 4δ); 7.22 (d, J = 5.5 Hz, 2H : H β of pyridine); 8.59 (d, J = 5.5 Hz, 2H : H α of pyridine).

Example Z

By carrying out the procedure as in Example Y but starting with 1.5 g of pristinamycin I_B and 640 mg of N-methyl-N-(1-methylpiperid-4-yl)bromoacetamide hydrobromide in 4.5 cm^3 of dry dimethylformamide and after stirring for 72 hours at room temperature, a solution is obtained after evaporation of a portion of the dimethylformamide at 50°C under a partial pressure, which solution is taken up in 15 cm^3 of distilled water. The reaction mixture is washed with twice 15 cm^3 of ethyl acetate. The aqueous phase is decanted off, adjusted to pH 5-6, washed again with ethyl acetate and then alkalinized to pH 8 with 0.1 N sodium hydroxide. The aqueous phase is supplemented with sodium chloride and then extracted with 15 cm^3 of methylene chloride. The organic phase is washed with 2 cm^3 of water,

decanted off, dried over magnesium sulphate, filtered and then concentrated under reduced pressure (2.7 kPa) to give 1.1 g of a pale-yellow solid which is dissolved in 30 cm^3 of a methylene chloride/methanol concentrated ammonia mixture (70/20/1 by volume) and then supplemented with 5.5 g of silica. After stirring for 45 minutes, the mixture is filtered, rinsed with twice the same volume of mixture of solvents and then concentrated to dryness. The product obtained is concreted from 15 cm^3 of ether and then filtered to give 680 mg of [N-(1-methylpiperid-4-yl)-N-methylamino-carbonylmethyl]pristinamycin I_B in the form of a white solid melting at 210°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): from 1.60 to 2.10 and from 2.75 to 3.00 (2 mts, respectively 6H and 2H : CH_2CH_2N of piperidine); 2.30 (s, 3H : NCH_3 of piperidine); 2.85 (s, 3H : $CONCH_3$); from 2.80 to 3.00 (mt, 1H : 1H of CH_2 at position 4β); 3.00 (s, 3H : $ArNCH_3$); 3.22 (s, 3H : NCH_3); 3.28 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 4.04 (s, 2H : $ArNCH_2$); 4.45 (mt, 1H : CONCH); 5.25 (dd, J = 12 and 4 Hz, 1H : 4α); 6.60 (d, J = 8.5 Hz, 2H : aromatic H at position 4ε); 7.00 (d, J = 8.5 Hz, 2H : aromatic H at position 4δ).

N-Methyl-N-(1-methylpiperid-4-yl)bromo-acetamide hydrobromide may be obtained in the following manner:

1.45 g of 1-methyl-4-methylaminopiperidine in

30 cm^3 of dry dimethylformamide are placed in a three-necked flask maintained under nitrogen at 5°C and then 0.95 g of bromoacetyl bromide dissolved in 10 cm^3 of chloroform is added over 1 hour. After 18 hours at room temperature, the reaction mixture is concentrated, the residue taken up in 30 cm^3 of ether and then stirred for 3 hours. The resulting solid is filtered, washed with ether and then dried under reduced pressure (2.7 kPa) to give 3.2 g of N-methyl-N-(1-methylpiperid-4-yl)-bromoacetamide hydrobromide in the form of a pale-yellow solid which is used as it is.

Example AA

By carrying out the procedure as in Example Y but starting with 2.4 g of pristinamycin I_B and 0.91 g of (1-ethoxycarbonylpiperid-4-yl)bromoacetamide in 7.5 cm^3 of dry dimethylformamide and after stirring for 96 hours at room temperature, a solution is obtained which is diluted with 80 cm^3 of distilled water. The mixture is adjusted to pH 8 with sodium bicarbonate, supplemented with sodium chloride and then extracted with twice 20 cm^3 of ethyl acetate. The aqueous phase is decanted off and then re-extracted with twice 20 cm^3 of ethyl acetate. The organic phases are pooled, dried over magnesium sulphate, filtered and then concentrated under reduced pressure (2.7 kPa) to give a pale-yellow solid which is taken up in ether to give after filtration and drying 2.6 g of a pale-yellow powder which is purified by flash chromatography (eluent:

dichloromethane-methanol 97/3) to give 1.1 g of [N-(1-ethoxycarbonylpiperid-4-yl)aminocarbonylmethyl]pristinamycin I_B in the form of a white solid melting at 195°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 1.23 (t, J = 7 Hz, CH_3 of ethyl); from 1.20 to 1.50 and from 1.70 to 1.95 (2 mts, 2H each : CH_2 of piperidine); 2.85 and from 3.90 to 4.15 (mt and unresolved complex respectively, 2H and 3H respectively : NCH_2 and NCH of piperidine); 2.95 (dd, J = 12.5 and 4 Hz, 1H : 1H of CH_2 at position 4β); 2.97 (s, 3H : $ArNCH_3$); 3.25 (s, 3H : NCH_3); 3.34 (t, J = 12.5 Hz, 1H : the other H of CH_2 at position 4β); 3.79 and 3.90 (2 d, J = 18 Hz, 1H each : $ArNCH_2$); 4.20 (q, J = 7 Hz, 2H : $COOCH_2$ of ethyl); 5.19 (dd, J = 12.5 and 4 Hz, 1H : 4α); 6.55 (mt, 1H : CONH); 6.63 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 7.15 (d, J = 8 Hz, 2H : aromatic H at position 4δ).

(1-Ethoxycarbonylpiperid-4-yl)bromoacetamide may be prepared in the following manner:

860 mg of 1-ethoxycarbonyl-4-aminopiperidine and then 15 cm^3 of dry chloroform (over amylene) and 0.84 cm^3 of triethylamine are placed in a three-necked flask maintained over nitrogen. The mixture is cooled to 5°C and then 0.48 cm^3 of bromoacetyl bromide dissolved in 2 cm^2 of dry chloroform is added over 45 minutes and the stirring is continued for 5 hours at room temperature. The chloroform is evaporated off under reduced pressure and the mixture taken up in

20 cm^3 of ethyl acetate and 120 cm^3 of distilled water. The organic phase is decanted off, washed with twice 5 cm^3 of water and then dried over magnesium sulphate, filtered, concentrated under reduced pressure (2.7 kPa) to give a pale-yellow solid which is taken up in ether to give after filtration and drying 970 mg of (1-ethoxycarbonylpiperid-4-yl)bromoacetamide in the form of a white powder which is used as it is.

Example AB

By carrying out the procedure as in Example Y but starting with 3 g of pristinamycin I_B and 1.53 g of N-(1-benzylpiperid-4-yl)bromoacetamide hydrobromide in 9 cm^3 of dry dimethylformamide and after stirring for 72 hours at room temperature, a solution is obtained which is diluted with 120 cm^3 of distilled water. The mixture is adjusted to pH 8 and then extracted with 3 times 30 cm^3 of ethyl acetate. The organic phase is decanted off, washed with 30 cm^3 of water and then dried over magnesium sulphate, filtered and then concentrated under reduced pressure (2.7 kPa) to give a pale-yellow solid which is taken up in ether to give after filtration and drying 3.3 g of a white powder which is purified by flash chromatography (eluent: dichloromethane-methanol 97/3) to give 0.95 g of [(1-benzylpiperid-4-yl)aminocarbonylmethyl]-pristinamycin I_B in the form of a white solid melting at 195°C.

^1H NMR spectrum (300 MHz, $CDCl_3$, δ in ppm):

from 1.35 to 1.65 and from 1.95 to 2.20 (2 mts, 2H each : CH_2 of piperidine); from 2.70 to 2.85 and from 3.25 to 3.40 (2 mts, 2H : NCH_2 of piperidine); 2.95 (dd, J = 12 and 4 Hz, 1H : 1H of CH_2 at position 4β); 2.97 (s, 3H : $ArNCH_3$); 3.26 (s, 3H : NCH_3); 3.35 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 3.47 (s, 2H : NCH_2Ar); 3.80 and 3.90 (2 d, J = 18 Hz, 1H each : $ArNCH_2$); from 3.75 to 3.95 (mt, 1H : NCH of piperidine); 5.25 (dd, J = 12 and 4 Hz, 1H : 4α); 6.50 (d, J = 7.5 Hz, 1H : CONH); 6.65 (d, J = 8.5 Hz, aromatic H at position 4ε); 7.15 (d, J = 8.5 Hz, 2H : aromatic H at position 4δ); from 7.15 to 7.40 (mt, 5H : aromatic H of benzyl).

N-(1-Benzylpiperid-4-yl)bromoacetamide hydrobromide may be obtained in the following manner:

950 mg of 4-amino-1-benzylpiperidine and then 15 cm^3 of dry chloroform (over amylene) are placed in a three-necked flask maintained under nitrogen. The mixture is cooled to 5°C and then 0.47 cm^3 of bromoacetyl bromide dissolved in 5 cm^3 of dry chloroform is added over 45 minutes and the stirring is continued for 30 minutes at 5°C. The chloroform is evaporated under reduced pressure and the mixture is taken up in 15 cm^3 of ether to give after filtration and drying 2 g of N-(1-benzylpiperid-4-yl)bromoacetamide hydrobromide in the form of a white powder which is used as it is.

Example AC

605 mg of [(1-benzylpiperid-4-yl)amino-

carbonylmethyl]pristinamycin I_B in 12 cm^3 of methanol and 6 cm^3 of dichloromethane, 120 mg of 10% palladium on carbon and then 0.22 cm^3 of 2.5 N hydrochloric ether are placed in a three-necked flask maintained under nitrogen. The mixture is placed under a hydrogen atmosphere at 18°C and then heated to 33°C. After 3 days the mixture is purged with nitrogen, filtered on Clarcel®, concentrated under reduced pressure and then taken up in 15 cm^3 of water. The solution is adjusted to pH 8 with 1 N sodium hydroxide, supplemented with sodium chloride and then extracted with dichloromethane. The organic phase is decanted off, washed with water saturated with sodium chloride, dried over magnesium sulphate, filtered and then concentrated under reduced pressure (2.7 kPa) to give a solid which is stirred for 18 hours in 11.2 cm^3 of 0.1 N hydrochloric acid. The medium is adjusted to pH 8 by addition of 11.2 cm^3 of 0.1 N sodium hydroxide and then supplemented with 3.6 g of sodium chloride. After stirring for 2 hours, the precipitate is filtered, rinsed with a minimum of ice-cold water and then taken up in ether. The solid is taken up in dichloromethane, dried over magnesium sulphate, filtered and then dried at 35°C under reduced pressure (90 Pa) to give 270 mg of [(4-piperidinyl)aminocarbonylmethyl]pristinamycin I_B in the form of a cream-coloured solid melting at 230°C.

^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): from 1.45 to 1.65 and from 1.80 to 2.00 (2 mts, 2H each

: CH_2 of piperidine); from 2.65 to 2.85 and from 3.05 to 3.25 (2 mts, 2H each : NCH_2 of piperidine); 2.95 (dd, J = 12 and 4 Hz, 1H : 1H of CH_2 at position 4β); 2.98 (s, 3H : $ArNCH_3$); 3.27 (s, 3H : NCH_3); 3.32 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 3.80 and 3.88 (2 d, J = 18 Hz, 1H each : $ArNCH_2$); 3.95 (mt, 1H : CONCH of piperidine); 5.22 (dd, J = 12 and 4 Hz, 1H : 4α); 6.63 (d, J = 8.5 Hz, 2H : aromatic H at position 4ε); 6.68 (d, J = 8 Hz, 1H : CONH); 7.10 (d, J = 8.5 Hz, 2H : aromatic H at position 4δ).

Example AD

15 g of pristinamycin I_A in 30 cm^3 of dry dimethylformamide are placed in a three-necked flask maintained under a nitrogen atmosphere and then 2.2 cm^3 of ethyl bromoacetate are added. The mixture is stirred for 22 hours at 80°C. After cooling, the reaction mixture is diluted with 300 cm^3 of distilled water and then stirred. The precipitate formed is filtered, rinsed with 3 times 50 cm^3 of distilled water and then with ether. The resulting solid is solubilized in ethyl acetate, filtered and then washed in a separating funnel with 3 times 50 cm^3 of distilled water. The organic phase is decanted off, dried over magnesium sulphate, filtered and then concentrated under reduced pressure (2.7 kPa) to give 7.2 g of a brown oil which is purified by flash chromatography (eluent: dichloromethane-methanol 98/2) to give 3.2 g of 4-N-(ethoxycarbonylmethyl]pristinamycin I_B in the form

of a white solid melting at 244°C.

^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 1.28 (t, J = 7 Hz, 3H : CH_3 of ethyl); 2.90 (dd, J = 12.5 and 4 Hz, 1H : 1H of CH_2 at position 4β); 3.05 (s, 3H : $ArNCH_3$); 3.26 (s, 3H : NCH_3); 3.34 (t, J = 12.5 Hz, 1H : the other H of CH_2 at position 4β); 4.02 and 4.08 (2 d, J = 18 Hz, 1H each : $ArNCH_2$); 4.20 (q, J = 7 Hz, 2H : CH_2 of ethyl); 5.22 (dd, J = 12.5 and 4 Hz, 1H : 4α); 6.62 (d, J = 8.5 Hz, 2H : aromatic H at position 4ε); 7.07 (d, J = 8.5 Hz, 2H : aromatic H at position 4δ).

Example AE

By carrying out the procedure as in Example AD but starting with 1.5 g of pristinamycin I_A in 3 cm^3 of dry dimethylformamide and 240 mg of bromoacetonitrile, 0.8 g of a white solid is obtained after 6 hours at 80°C which is purified by flash chromatography (eluent: dichloromethane-methanol 97/3) to give 0.48 g of 4-N-cyanomethylpristinamycin I_B in the form of a white solid melting at 258°C.

^{1}H NMR spectrum (300 MHz, $CDCl_3$, δ in ppm): 2.95 (dd, J = 12 and 4 Hz, 1H : 1H of CH_2 at position 4β); 2.97 (s, 3H : $ArNCH_3$); 3.20 (s, 3H : NCH_3); 3.32 (t, J = 12 Hz, 1H : the other H of CH_2 at position 4β); 4.10 (limiting AB, J = 18 Hz, 2H : $ArNCH_2$); 5.23 (dd, J = 12 and 4 Hz, 1H : 4α); 6.75 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 7.09 (d, J = 8 Hz, 2H : aromatic H at position 4δ).

Example AF

5δ-Methylenepristinamycin I_B may be obtained in the following manner.

10 cm^3 of methanol and 1 cm^3 of morpholine are placed in a three-necked flask maintained under a nitrogen atmosphere and then 0.6 cm^3 of methanesulphonic acid is slowly added while the temperature is maintained below 20°C. 0.17 g of polyoxymethylene and then 1 g of pristinamycin I_B are then added with stirring. The milky suspension obtained is heated for 4 hours at 40°C and then stirred for 12 hours at room temperature. The mixture is concentrated to dryness, taken up in 20 cm^3 of ethyl acetate and 20 cm^3 of distilled water, filtered on Clarcel® and then decanted off. The aqueous phase is extracted with twice 10 cm^3 of ethyl acetate and then the organic phases are pooled, washed with 30 cm^3 of an aqueous solution of sodium chloride, decanted off, dried over sodium sulphate and then concentrated under reduced pressure (2.7 kPa) to a volume of 50 cm^3. The organic phase of 50 cm^3 thus concentrated is added, in a three-necked flask, with stirring, to 35 cm^3 of distilled water, 1.3 cm^3 of acetic acid and 0.16 g of sodium acetate trihydrate. The mixture is heated for 3 hours at 40-45°C and then after cooling, a saturated sodium bicarbonate solution is added to a pH of 5-6. The aqueous phase is decanted off, extracted with 20 cm^3 of ethyl acetate and then the organic phases are combined and washed with 30 cm^3 of

bicarbonated distilled water. The aqueous phase is decanted off and then extracted with 20 cm^3 of ethyl acetate. All the organic phases are pooled, washed with a saturated aqueous sodium chloride solution, dried over sodium sulphate, filtered and concentrated to dryness under reduced pressure to give 1.03 g of a solid which is purified by two successive flash chromatographies (eluent: methylene chloride-methanol 96/4) to give 0.21 g of a product which is concreted from 5 cm^3 of diethyl ether. After filtration and drying at 50°C under reduced pressure (90 Pa), 169 mg of 5δ-methylenepristinamycin I_B are obtained in the form of an off-white solid melting at 210°C (not very sharp).

^1H NMR spectrum (300 MHz, $CDCl_3$, δ in ppm): 0.66 (dd, J = 16.5 and 6 Hz, 1H : 1H of CH_2 at position 5β); 0.91 (t, J = 7.5 Hz, 3H : CH_3 at position 2γ); from 1.15 to 1.35 (mt, 2H : 1H of CH_2 at position 3β and 1H of CH_2 at position 3γ); 1.33 (d, J = 7 Hz, 3H : CH_3 at position 1γ); from 1.50 to 1.85 (mt : 3H corresponding to the other H of CH_2 at position 3γ and to the CH_2 at position 2β); 2.03 (mt, 1H : the other H of CH_2 at position 3β); 2.50 (d, J = 16.5 Hz, 1H : the other H of CH_2 at position 5β); 2.81 (s, 3H : $ArNCH_3$); 2.88 (dd, J = 12 and 4.5 Hz, 1H : 1H of CH_2 at position 4β); from 3.20 to 3.35 (mt, 2H : 1H of CH_2 at position 3δ and the other H of CH_2 at position 4β); 3.26 (s, 3H : NCH_3); 3.52 (mt, 1H : the other H of CH_2 at position 3δ); 3.59 (broad d, J = 16.5 Hz, 1H : 1H of CH_2 at position 5ε);

from 3.65 to 3.90 (broad unresolved complex, 1H : ArNH); 4.60 (dd, J = 9 and 6 Hz, 1H : CH at position 3α); 4.82 (mt, 1H : CH at position 2α); 4.88 (dd, J = 10 and 1 Hz, 1H : CH at position 1α); 5.05 (dd, J = 12 and 4.5 Hz, 1H : CH at position 4α); 5.28 (broad d, J = 16.5 Hz, 1H : the other H of CH_2 at position 5ε); 5.28 (d, J = 6 Hz, 1H : CH at position 5α); 5.35 and 6.17 (2 broad s, 1H each : $=CH_2$); 5.84 (d, J = 9 Hz, 1H : CH at position 6α); 5.90 (dq, J = 7 and 1 Hz, CH at position 1β); 6.46 (d, J = 8 Hz, 2H : aromatic H at position 4ε); 6.50 (d, J = 10 Hz, CONH at position 2); 6.91 (d, J = 8 Hz, 2H : aromatic H at position 4δ); from 7.15 to 7.35 (mt: the 5 aromatic H at position 6); 7.47 (limiting AB, 2H : 1'H_4 and 1'H_5); 7.82 (dd, J = 4 and 2 Hz, 1H : 1'H_6); 8.38 (d, J = 10 Hz, 1H : CONH at position 1); 8.73 (d, J = 9 Hz, 1H : CONH at position 6); 11.60 (s, 1H : OH).

The products of the above examples may be treated by analogy with the methods described in Examples 1 to 33 in order to prepare the streptogramin derivatives of general formula (I).

The present invention also relates to the pharmaceutical compositions containing at least one streptogramin derivative according to the invention, in the pure state, combined with at least one group A streptogramin derivative, where appropriate in salt form, and/or in the form of a combination with one or more compatible and pharmaceutically acceptable

diluents or adjuvants.

The compositions according to the invention may be used by the oral, parenteral, topical or rectal route or in the form of aerosols.

As solid compositions for oral administration, tablets, pills, gelatin capsules, powders or granules may be used. In these compositions, the active product according to the invention, generally in the form of a combination, is mixed with one or more inert diluents or adjuvants, such as sucrose, lactose or starch. These compositions may comprise substances other than diluents, for example a lubricant such as magnesium stearate or a coating intended for a controlled release.

As liquid compositions for oral administration, there may be used solutions which are pharmaceutically acceptable, suspensions, emulsions, syrups and elixirs containing inert diluents such as water or paraffin oil. These compositions may also comprise substances other than diluents, for example wetting, sweetening or flavouring products.

Compositions for parenteral administration may be emulsions or sterile solutions. As solvent or vehicle, there may be used propylene glycol, a polyethylene glycol, vegetable oils, in particular olive oil, or injectable organic esters, for example ethyl oleate. These compositions may also contain adjuvants, in particular wetting, isotonizing,

emulsifying, dispersing and stabilizing agents.

Sterilization may be carried out in several ways, for example with the aid of a bacteriological filter, by irradiation or by heating. They may also be prepared in the form of sterile solid compositions which may be dissolved at the time of use in sterile water or any other injectable sterile medium.

Compositions for topical administration may be, for example, creams, ointments, lotions or aerosols.

Compositions for rectal administration are suppositories or rectal capsules which contain, in addition to the active ingredient, excipients such as cocoa butter, semisynthetic glycerides or polyethylene glycols.

The compositions may also be aerosols. For use in the form of liquid aerosols, the compositions may be stable sterile solutions or solid compositions which are dissolved at the time of use in apyrogenic sterile water, in saline or any other pharmaceutically acceptable vehicle. For use in the form of dry aerosols intended to be directly inhaled, the active ingredient is finely divided and combined with a water-soluble solid diluent or vehicle with a particle size distribution of 30 to 80 µm, for example dextran, mannitol or lactose.

In human therapy, the new streptogramin derivatives according to the invention are particularly

useful in the treatment of infections of bacterial origin. The doses depend on the desired effect and the duration of treatment. The doctor will determine the dosage which he judges to be the most appropriate depending on the treatment, depending on the age, weight and degree of infection and other factors specific to the subject to be treated. Generally, the doses are between 1 and 3 g of active product in 2 or 3 doses per day orally for an adult.

The following example illustrates a composition according to the invention.

EXAMPLE

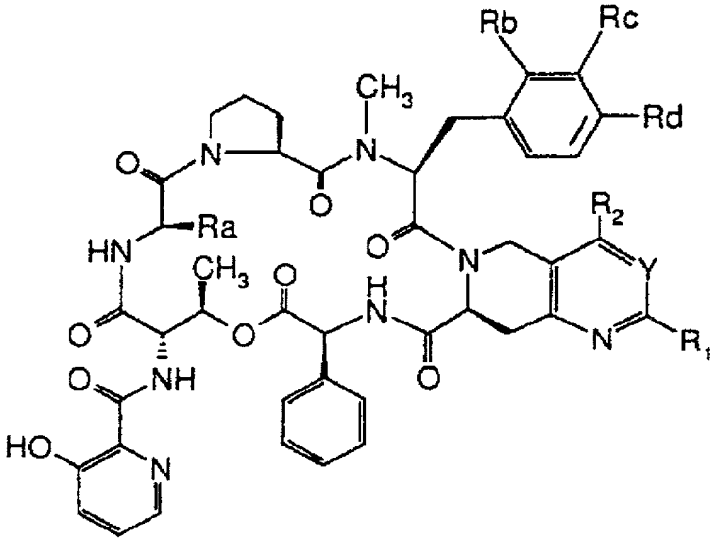
Tablets containing a dose of 250 mg of active ingredient and having the following composition are prepared according to the usual technique:

- 2"-methylpyrido[2,3-5γ,5δ]pristinamycin I_E .. 75 mg
- pristinamycin II_B..... 175 mg
- excipient: starch, hydrated silica, dextrin, gelatin, magnesium stearate: qs..... 500 mg

CLAIMS

What is claimed is:

1. A group B streptogramin derivative of general formula:



(I)

in which

Y is a nitrogen atom or a radical $=CR_3-$,

R_1 is a hydrogen atom, a radical alkyl (1 to 8 carbons), alkenyl (2 to 8 carbons), cycloalkyl (3 to 8 carbons), heterocyclyl which is saturated or unsaturated (3 to 8 members), phenyl, phenyl which is substituted (with one or more halogen atoms or hydroxyl, alkyl, alkyloxy, alkylthio, alkylsulphinyl, alkylsulphonyl, amino, alkylamino or dialkylamino radicals) or a radical NR'R", R' and R", which are identical or different, being capable of being hydrogen atoms or alkyl radicals (1 to 3 carbons), or being capable of forming together with the nitrogen atom to which they are attached a 3-

to 8-membered heterocycle optionally containing another heteroatom chosen from oxygen, sulphur or nitrogen which is optionally substituted (with a radical alkyl, alkenyl (2 to 8 carbons), cycloalkyl (3 to 6 carbons), heterocyclyl which is saturated or unsaturated (4 to 6 members), benzyl, phenyl or phenyl which is substituted as defined above for the definition of R_1),

or alternatively when Y is a radical $=CR_3-$, R_1 may also be halomethyl, hydroxymethyl, alkyloxymethyl, alkylthiomethyl in which the alkyl portion is optionally substituted with NR'R", alkylsulphinylmethyl, alkylsulphonylmethyl, acyloxymethyl, benzoyloxymethyl, cyclopropylaminomethyl or $-(CH_2)_nNR'R"$ (n being an integer from 1 to 4 and R' and R" being defined as above), or alternatively if R_3 is a hydrogen atom, R_1 may also be formyl, carboxyl, alkyloxycarbonyl, or -CONR'R" for which R' and R" are defined as above,

or alternatively when Y is a nitrogen atom, R_1 may also be a radical $-XR^o$ for which X is an oxygen or sulphur atom, a sulphinyl or sulphonyl radical, or an NH radical and R^o is a radical alkyl (1 to 8 carbons), cycloalkyl (3 to 6 carbons), heterocyclyl which is saturated or unsaturated (3 to 8 members), heterocyclylmethyl (3 to 8 members) in which the heterocyclyl portion is attached to the methyl radical by a carbon atom, phenyl, phenyl which is substituted (with one or more halogen atoms or hydroxyl, alkyl,

alkyloxy, alkylthio, alkylsulphinyl, alkylsulphonyl, amino, alkylamino or dialkylamino radicals) or a radical $-(CH_2)_nNR'R"$ for which R' and R" are defined as above and n is an integer from 2 to 4, or alternatively if X represents NH, R^o may also represent the hydrogen atom,

R_2 is a hydrogen atom or an alkyl radical (1 to 3 carbons),

R_3 is a hydrogen atom or an alkyl, carboxyl, alkyloxycarbonyl or carbamoyl radical having the structure -CO-NR'R" in which R' and R" are defined as above,

Ra is a methyl or ethyl radical, and

Rb, Rc and Rd have the definitions below:

1) Rb and Rc are hydrogen atoms and Rd is a hydrogen atom or a methylamino or dimethylamino radical,

2) Rb is a hydrogen atom, Rc is a hydrogen, chlorine or bromine atom, or represents an alkenyl radical (3 to 5C), and Rd is a radical -NMe-R''' for which R''' represents a radical alkyl, hydroxyalkyl (2 to 4C), or alkenyl (2 to 8C) which is optionally substituted with phenyl, cycloalkyl(3 to 6C) methyl, benzyl, benzyl which is substituted (with one or more halogen atoms or hydroxyl, alkyl, alkyloxy, alkylthio, alkylsulphinyl, alkylsulphonyl, amino, alkylamino or dialkylamino radicals), heterocyclylmethyl or heterocyclylethyl in which the heterocyclyl portion is saturated or

unsaturated and contains 5 to 6 members and 1 or 2 heteroatoms chosen from sulphur, oxygen or nitrogen which is optionally substituted (with a radical alkyl, alkenyl (2 to 8 carbons), cycloalkyl (3 to 6 carbons), heterocyclyl which is saturated or unsaturated (4 to 6 members), phenyl, phenyl which is substituted as defined above for the definition of R_1 or benzyl), or alternatively R''' represents a radical cyanomethyl, or $-CH_2CORe$ for which either Re is -OR'e, R'e being hydrogen, alkyl (1 to 6 carbons), alkenyl (2 to 6 carbons), benzyl or heterocyclylmethyl in which the heterocyclyl portion contains 5 to 6 members and 1 or 2 heteroatoms chosen from sulphur, oxygen or nitrogen, or Re is an alkylamino, alkylmethylamino, heterocyclylamino or heterocyclylmethylamino radical in which the heterocyclyl portion is saturated and contains 5 to 6 members and 1 or 2 heteroatoms chosen from sulphur, oxygen or nitrogen which is optionally substituted with an alkyl, benzyl or alkyloxycarbonyl radical,

3) Rb is a hydrogen atom, Rd is a radical $-NHCH_3$ or $-N(CH_3)_2$ and Rc is a chlorine or bromine atom, or represents an alkenyl radical (3 to 5C), (if Rd is $-N(CH_3)_2$),

4) Rb and Rd are hydrogen atoms and Rc is a halogen atom, or an alkylamino or dialkylamino, alkyloxy,

trifluoromethoxy, thioalkyl, alkyl (1 to 6C) or trihalomethyl radical,

5) Rb and Rc are hydrogen atoms and Rd is a halogen atom, or an ethylamino, diethylamino or methylethylamino, alkyloxy or trifluoromethoxy, alkylthio, alkylsulphinyl, alkylsulphonyl, alkyl (1 to 6C), phenyl or trihalomethyl radical,

6) Rb is a hydrogen atom and Rc is a halogen atom or an alkylamino or dialkylamino, alkyloxy or trifluoromethoxy, thioalkyl or alkyl (1 to 3C) radical, and Rd is a halogen atom or an amino, alkylamino or dialkylamino, alkyloxy or trifluoromethoxy, thioalkyl, alkyl (1 to 6C) or trihalomethyl radical,

7) Rc is a hydrogen atom and Rb and Rd represent a methyl radical,

the alkyl, alkenyl or acyl radicals being straight or branched and, unless otherwise stated, the alkyl or acyl radicals containing 1 to 4 carbon atoms, as well as its salts when they exist.

2. A group B streptogramin derivative according to claim 1, wherein

Y is a nitrogen atom or a radical $=CR_3-$,

R_1 is a hydrogen atom, a radical alkyl (1 to 8 carbons), cycloalkyl (3 to 8 carbons), heterocyclyl which is saturated or unsaturated (3 to 8 members), phenyl, phenyl which is substituted (with one or more amino,

alkylamino or dialkylamino radicals) or a radical NR'R", R' and R", which are identical or different, being capable of being hydrogen atoms or alkyl radicals (1 to 3 carbons), or being capable of forming together with the nitrogen atom to which they are attached a 3- to 8-membered heterocycle optionally containing another heteroatom chosen from oxygen, sulphur or nitrogen which is optionally substituted with an alkyl radical,

or alternatively when Y is a radical $=CR_3-$, R_1 may also be halomethyl, hydroxymethyl, alkylthiomethyl in which the alkyl portion is optionally substituted with NR'R", alkylsulphinylmethyl, alkylsulphonylmethyl, acyloxymethyl, cyclopropylaminomethyl or $-(CH_2)_nNR'R"$ (n being an integer from 1 to 4 and R' and R" being defined as above), or alternatively if R_3 is a hydrogen atom, R_1 may also be formyl or -CONR'R" for which R' and R" are defined as above,

or alternatively when Y is a nitrogen atom, R_1 may also be a radical $-XR^\circ$ for which X is an oxygen or sulphur atom, a sulphinyl or sulphonyl radical, or an NH radical and R° is a radical alkyl (1 to 8 carbons), heterocyclylmethyl (3 to 8 members) in which the heterocyclyl portion is attached to the methyl radical by a carbon atom, or a radical $-(CH_2)_nNR'R"$ for which R' and R" are defined as above and n is an integer from 2 to 4,

R_2 is a hydrogen atom or an alkyl radical (1 to 3 carbons),

R_3 is a hydrogen atom or a carboxyl or alkyloxycarbonyl radical,

Ra is a methyl or ethyl radical, and

Rb, Rc and Rd have the definitions below:

- Rb and Rc are hydrogen atoms and Rd is a hydrogen atom or a methylamino or dimethylamino radical,
- Rb is a hydrogen atom, Rd is a radical $-NHCH_3$ or $-N(CH_3)_2$ and Rc is a chlorine or bromine atom,

as well as its salts when they exist.

3. A group B streptogramin derivative according to claim 1, wherein

Y is a nitrogen atom or a radical $=CR_3-$,

R_1 is a hydrogen atom, a radical alkyl (1 to 3 carbons), cycloalkyl (3 to 8 carbons), heterocyclyl which is saturated or unsaturated (3 to 8 members), phenyl, phenyl which is substituted with an amino radical, or alternatively when Y is a radical $=CR_3-$, R_1 may also be acyloxymethyl,

or alternatively when Y is a nitrogen atom, R_1 may also be a radical $-XR^o$ for which X is an oxygen or sulphur atom or a radical NH and R^o is an alkyl radical (1 to 4 carbons) or a radical $-(CH_2)_nNR'R"$ for which R' and R" which are identical or different may be hydrogen atoms or alkyl radicals (1 to 3 carbons), or form together with the nitrogen atom to which they are attached a 3- to 8-membered heterocycle optionally containing another heteroatom chosen from oxygen, sulphur or nitrogen

optionally substituted with an alkyl radical, and n is an integer from 2 to 4,

R_2 is a hydrogen atom or an alkyl radical (1 to 3 carbons),

R_3 is a hydrogen atom or an alkyloxycarbonyl radical,

Ra is a methyl or ethyl radical, and

Rb, Rc and Rd have the definitions below:

- Rb and Rc are hydrogen atoms and Rd is a hydrogen atom or a methylamino or dimethylamino radical,
- Rb is a hydrogen atom, Rd is a radical $-NHCH_3$ or $-N(CH_3)_2$ and Rc is a chlorine atom,

as well as its salts when they exist.

4. A group B streptogramin derivative according to claim 1, which is 2"-methylpyrido[2,3-5γ,5δ]pristinamycin I_E.

5. A group B streptogramin derivative according to claim 1, which is 2"-cyclopropylpyrido[2,3-5γ,5δ]pristinamycin I_E.

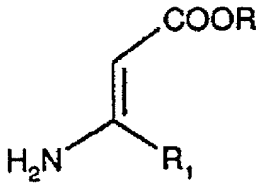
6. A group B streptogramin derivative according to claim 1, which is pyrido[2,3-5γ,5δ]pristinamycin I_E.

7. A group B streptogramin derivative according to claim 1, which is

2"-ethylpyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E.

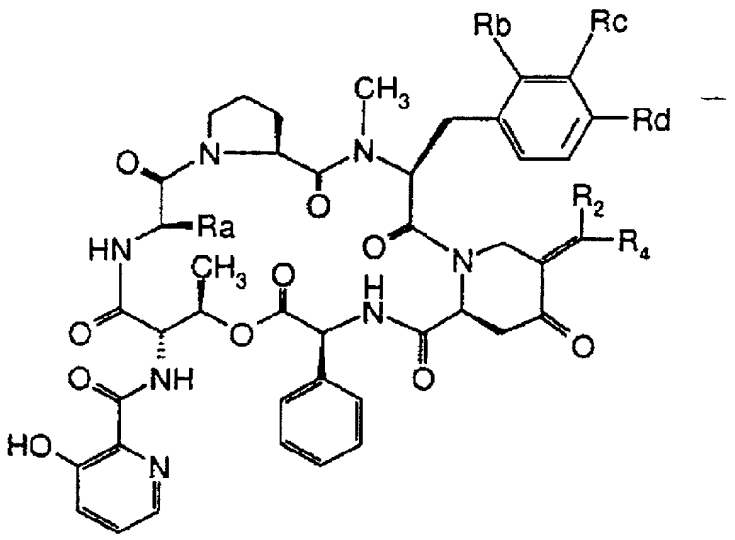
8. A group B streptogramin derivative according to claim 1, which is 4ε-chloro-2"-(ethyl)-pyrido[2,3-5γ,5δ](4ζ-methylamino)-(4ζ-dedimethylamino)pristinamycin I_E.

9. A process for the preparation of a streptogramin derivative according to claim 1, wherein Y is a radical $=CR_3-$ and R_3 is other than an alkyl radical, wherein an enamino ester of general formula:



(II)

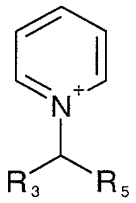
in which R_1 is defined as above and R represents the residue of an easily hydrolysable ester or an alkyl radical, is reacted with the corresponding 5δ-methylenepristinamycin derivative of general formula:



(III)

in which Ra, Rb, Rc and Rd are defined as for claim 1, R_2 is defined as for claim 1 and R_4 is a hydrogen atom, or R_2 represents a hydrogen atom and R_4 is a hydrogen atom or a dialkylamino radical, followed where appropriate by the conversion of the ester obtained to an acid, and then optionally by its decarboxylation, or by the conversion of the acid to a carbamoyl radical according to the derivative according to claim 1 desired, and/or followed where appropriate by the conversion of the derivative according to claim 1 for which R_1 is hydroxymethyl to a derivative for which R_1 is a radical formyl, and then where appropriate carboxyl, and then where appropriate alkyloxycarbonyl or -CONR'R" and/or optionally followed by the mono-N-demethylation of the derivative according to claim 1 for which Rd is a dimethylamino radical to a derivative for which Rd is methylamino, and then optionally followed by the conversion to a salt when they exist.

10. A process for the preparation of a streptogramin derivative according to claim 1, for which Y is a radical $=CR_3-$ and R_3 is a hydrogen atom or an alkyl radical, wherein a pyridinium salt of general formula:

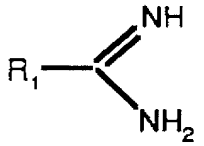


X^- (IV)

in which R_3 is defined as above, R_5 is the residue of a ketone R_1-CO- for which R_1 is defined as above with the exception of representing a radical -NR'R", or optionally represents a protected hydroxyl radical or a nitrophenyl radical or alternatively R_5 represents the cyano radical so as to obtain a streptogramin derivative for which R_1 is an amino radical, and X^- is an anion, is reacted with the corresponding 5δ-methylenepristinamycin derivative of general formula (III) defined in claim 2, in which R_4 is a hydrogen atom and Ra, Rb, Rc, Rd and R_2 are defined as for claim 1, optionally followed by the liberation of the hydroxyl radical or where appropriate the reduction of the nitrophenyl radical so as to obtain a derivative for which R_1 is an aminophenyl radical, or optionally followed by the reaction of an amine of general formula HNR'R" with the streptogramin derivative according to claim 1, for which R_1 is halomethyl, so as to obtain the corresponding derivative for which R_1 is a radical $-CH_2NR'R"$, or where appropriate by the conversion of the

derivative according to claim 1 for which R_1 is hydroxymethyl to a derivative for which R_1 is a radical formyl, and then where appropriate carboxyl, and then where appropriate alkyloxycarbonyl or -CONR'R" and/or optionally the mono-N-demethylation of the derivative according to claim 1 for which Rd is a dimethylamino radical to a derivative for which Rd is methylamino, and then optionally followed by the conversion to a salt, when they exist.

11. A process for the preparation of a streptogramin derivative according to claim 1, for which Y is a nitrogen atom, wherein an amidine salt or a derivative of isourea or of isothiourea of general formula:

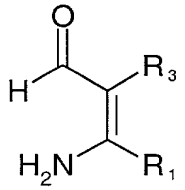


(V)

in which R_1 is defined as for claim 1, with the exception of representing a radical XR^o for which X is sulphonyl or sulphinyl, or a radical NR'R" other than amino, is reacted with a streptogramin derivative of general formula (III) as defined in claim 2, for which R_4 is dialkylamino, and then in order to obtain a streptogramin derivative according to claim 1, for which R_1 is a radical XR^o for which X is sulphonyl or sulphinyl, the corresponding derivative for which X is a sulphur atom is oxidized, and then in order to obtain

the streptogramin derivative according to claim 1, for which R_1 is a radical NR'R", the sulphonyl derivative obtained is substituted by the action of the corresponding amine HNR'R" and/or optionally in order to obtain a derivative for which Rd is methylamino, the mono-N-demethylation of the derivative according to claim 1, for which Rd is a dimethylamino radical is carried out, and then optionally converted to a salt, when they exist.

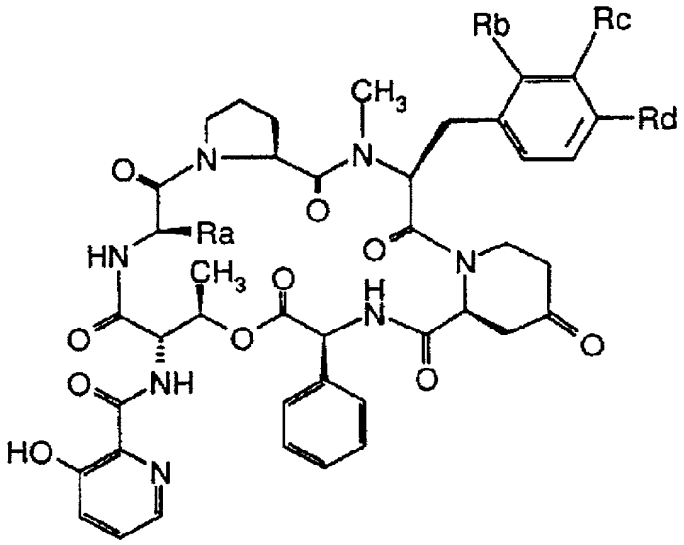
12. A process for the preparation of a streptogramin derivative according to claim 1, for which Y is a radical $=CR_3-$, R_1 is a hydrogen atom, an alkyl, alkenyl, cycloalkyl, aromatic heterocyclyl, phenyl, substituted phenyl, halomethyl, hydroxymethyl, alkyloxymethyl, alkylthiomethyl, alkylsulphinylmethyl, alkylsulphonylmethyl or $-(CH_2)_nNR'R"$ radical, or alternatively when R_3 is a hydrogen atom, for which R_1 is formyl, carboxyl, alkyloxycarbonyl or -CONR'R" as defined for claim 1 and R_2 is a hydrogen atom, wherein the formyl enamine of general formula:



(VI)

in which R_1 is a hydrogen atom, an alkyl, alkenyl, cycloalkyl, aromatic heterocyclyl, phenyl, substituted phenyl, hydroxymethyl, alkyloxymethyl, alkylthiomethyl

or $-(CH_2)_nNR'R"$ radical and R_3 is defined as for claim 1, with the exception of representing carboxyl, is reacted with a streptogramin derivative of general formula:

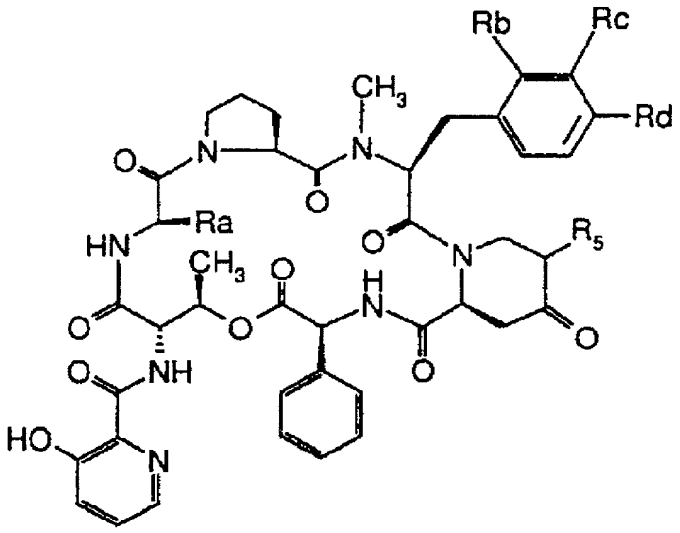


in which Ra, Rb, Rc and Rd are defined as for claim 1, followed where appropriate by the conversion of the derivative for which R_3 is amide or ester to a derivative for which R_3 is carboxyl and/or where appropriate the oxidation of the derivative for which R_1 is alkylthiomethyl to a derivative for which R_1 is alkylsulphinylmethyl or alkylsulphonylmethyl, or where appropriate the conversion of the derivative for which R_1 is a hydroxymethyl radical to a derivative for which R_1 is halomethyl, and then where appropriate the conversion of the derivative for which R_1 is halomethyl to a derivative for which R_1 is $-CH_2NR'R"$, or where appropriate the conversion of the derivative according to claim 1, for which R_1 is hydroxymethyl to a derivative for which R_1 is a radical formyl, and then

where appropriate carboxyl, alkyloxycarbonyl and/or -CONR'R", and/or optionally the mono-N-demethylation of the derivative according to claim 1, for which Rd is a dimethylamino radical to a derivative for which Rd is methylamino, and then optionally followed by conversion to a salt, when they exist.

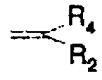
13. A process for the preparation of a streptogramin derivative according to claim 1, for which Rd is methylamino, wherein the mono-N-demethylation of the derivative according to claim 1, for which Rd is a dimethylamino radical, is carried out and then the streptogramin derivative obtained is optionally converted to a salt.

14. A streptogramin derivative of general formula:



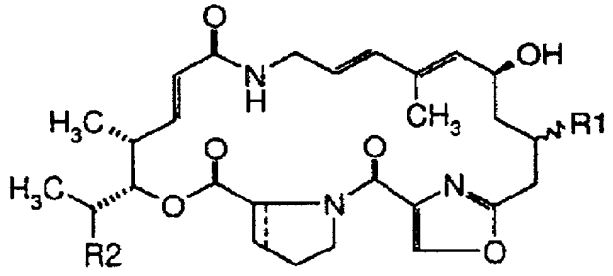
(IX)

in which Ra is a methyl radical and Rb, Rc and Rd are defined as in claim 1, or Ra is an ethyl radical and

Rb, Rc and Rd are defined as in claim 1 in 2) to 7) and R_5 represents a disubstituted methylenyl radical having the structure  for which R_2 and R_4 are defined as above, or alternatively in which Ra, Rb, Rc and Rd are defined as for claim 1 in 2), except for R"' representing ethyl if Rb and Rc are hydrogen, and R_5 is a hydrogen atom.

15. A pharmaceutical composition comprising a group B streptogramin derivative according to claim 1, in a pure state or in the form of a combination with at least one group A streptogramin derivative, where appropriate in the form of a salt, and/or in the form of a combination with one or more compatible and pharmaceutically acceptable diluents or adjuvants.

16. A pharmaceutical composition according to claim 15, wherein the group A streptogramin derivative is chosen from pristinamycin II_A, pristinamycin II_B, pristinamycin II_C, pristinamycin II_D, pristinamycin II_E, pristinamycin II_F, pristinamycin II_G or from known semisynthetic derivatives or from the derivatives of general formula:



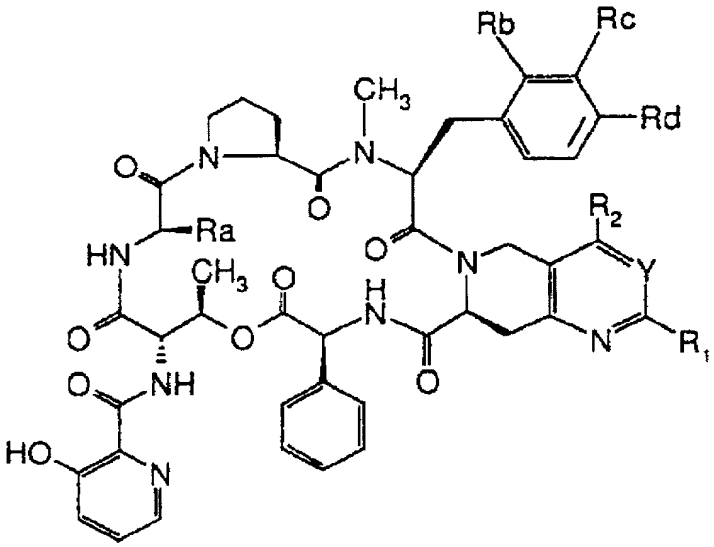
(α)

in which R_1 is a radical -NR'R" for which R' is a hydrogen atom or a methyl radical, R" is a hydrogen atom, an alkyl, cycloalkyl, allyl, propargyl, benzyl or -OR''', R''' radical being a hydrogen atom, an alkyl, cycloalkyl, allyl, propargyl or benzyl radical, or $-NR_3R_4$, it being possible for R_3 and R_4 to represent a methyl radical, or to form together with the nitrogen atom to which they are attached a saturated or unsaturated 4- or 5-membered heterocycle which may in addition contain another heteroatom chosen from nitrogen, oxygen or sulphur, R_2 is a hydrogen atom or a methyl or ethyl radical, and the bond <u>---</u> represents a single bond or a double bond, as well as their salts.

17. A combination of a group B streptogramin derivative according to claim 1 with at least one group A streptogramin derivative as defined in claim 16.

ABSTRACT

Group B streptogramin derivatives of general formula (I):



(I)

wherein Ra, Rb, Rc, Rd, R_1, R_2 and Y are as defined in the description, including preparation methods and compositions containing same. Such derivatives are particularly useful as antimicrobial agents, optionally combined with at least one group A streptogramin derivative.

DECLARATION AND POWER OF ATTORNEY
FOR PATENT APPLICATION

As a below named inventor, I hereby declare that my residence, post office address and citizenship are as stated below next to my name; I believe that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

STREPTOGRAMIN DERIVATIVES, PREPARATION METHOD AND COMPOSITIONS CONTAINING SAME

the specification, assigned Attorney Docket No. ST98007-US , of which (check one):
x is attached hereto; ___ was filed on _____, as Application Serial No. _____, and was amended on (or amended through) _____ (if applicable). I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment(s) referred to above. I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, Section 1.56(a). I hereby claim foreign priority benefits under Title 35, United States Code, Section 119(a)-(d) or Section 365 (b) of a foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed.

Prior Foreign Applications(s)			Priority Claimed	
98/02316	France	26/02/98	x	
(Number)	(Country)	(Day/Month/Year Filed)	Yes	No

I hereby claim priority benefits under Title 35, United States Code, Section 119(e) of any United States provisional application(s) listed.

Prior US Provisional Applications(s)

(Number)	(Day/Month/Year Filed)

I hereby claim the benefit under Title 35, United States Code, Section 120 of any United States application(s), or Section 365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application or PCT international application in the manner provided by the first paragraph of Title 35, United States Code, Section 112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, Section 1.56 which occurred between the filing date of the prior application and the national or PCT International filing date of this application:

(Application Serial No.)	(Filing Date)	(Status-Patented, Pending or Abandoned)
PCT/FR99/00409	February 24, 1999	Completed
(Application Serial No.)	(Filing Date)	(Status-Patented, Pending or Abandoned)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

POWER OF ATTORNEY: I (We) hereby appoint the attorneys associated with the Customer Number provided below as my (our) attorneys, with full powers of substitution and revocation, to prosecute this application and transact all business in the Patent and Trademark Office connected therewith:

Customer No.:	005487
Direct Telephone Calls to:	(908) 231-2972

Pascal Desmazeau	French
First or Sole Inventor	Citizenship
45 rue des Marronniers	Same
Residence Address	Post Office Address
Tigery	Same
City	City
France 91250	Same
State (Zip) or Country	State (Zip) or Country
Date	Signature

Gilles Doerflinger Second Inventor	French Citizenship
Résidence Les Millepertuis, Bât. B3 Residence Address	Same Post Office Address
Les Ulis City	Same City
France 91940 State (Zip) or Country	Same State (Zip) or Country
Date	Signature

Yves Ribeill Third Inventor	French Citizenship
313 Meeting House Circle Residence Address	Same Post Office Address
Raleigh City	Same City
North Carolina 27615 State (Zip) or Country	Same State (Zip) or Country
Date	Signature

Eric Bacque	French
Fourth Inventor	Citizenship
19 rue Colas	Same
Residence Address	Post Office Address
Morsang Sur Orge	Same
City	City
France 91390	Same
State (Zip) or Country	State (Zip) or Country
Date	Signature

Jean-Claude Barriere	French
Fifth Inventor	Citizenship
24 rue Max Ernst	Same
Residence Address	Post Office Address
Bures Sur Yvette	Same
City	City
France 91400	Same
State (Zip) or Country	State (Zip) or Country
Date	Signature

Gilles Dutruc-Rosset Sixth Inventor	French Citizenship
21 avenue du docteur Arnold Netter Residence Address	Same Post Office Address
Paris City	Same City
France 75012 State (Zip) or Country	Same State (Zip) or Country
Date	Signature

Gérard Puchault Seventh Inventor	French Citizenship
7 rue des Marguilliers Residence Address	Same Post Office Address
Marcilly City	Same City
France 77139 State (Zip) or Country	Same State (Zip) or Country
Date	Signature